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### Determinants of patient delay in doctor consultation in head and neck cancers (Protocol DEREDIA)

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# Determinants of patient delay in doctor consultation in head and neck cancers (Protocol DEREDIA)

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## Abstract

**Background:** Reducing the time between the onset of the first symptoms of cancer and the first consultation with a doctor (patient delay) is essential to improve the vital prognosis and quality of life of patients. Longer patient delay is linked to already known socio-demographic, socio-economic, socio-educational, socio-cultural, and socio-professional factors. However, recent data suggest that some socio-cognitive and emotional determinants may explain patient delay from a complementary point of view. The main objective of this study is to assess whether, in head and neck cancer, patient delay is linked to these socio-cognitive and emotional factors, in addition to previously known factors.

**Methods/design:** We intend to include in this study 400 patients with a not yet treated head and neck cancer diagnosed in one of six health centers in the North of France region. The main evaluation criterion is "patient delay". Socio-cognitive, emotional, medical, socio-demographic, socio-economic, educational, professional and geographic factors will be assessed by means of (1) a case report form, (2) a questionnaire completed by the clinical research associate together with the patient, (3) a questionnaire completed by the patient, and (4) a recorded semi-directive interview of the patient by a psychologist (for 80 patients only). The collected data will be analyzed to underline the differences between patients who consulted a doctor earlier versus those who consulted later.

**Discussion:** This study aims to identify some new determinants of patient delay. According to the results, interventional studies may be carried out and some measures targeting "at risk" people may thus be implemented. The final purpose will be to reduce patient delay in order to (1) decrease high death rates and quality of life impairments caused by medical care delays, and (2) fight social inequalities regarding health.

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## Background

The time between the onset of the first symptoms and the effective treatment of patients with cancer seems to be a decisive factor in the vital prognosis of patients [1-2] and in the psychological adjustment of patients and their relatives [3]. Reducing mortality related to avoidable cancers therefore implies reducing the timeline between the initial diagnosis of the disease and the start of medical treatment. In addition to the time required for the prescription of medical examinations, the carrying out of examinations, the diagnosis of cancer, and treatment initiation, the delay between the onset of the first symptoms and the patient's consultation with a doctor seems to be a decisive factor in survival and quality of life [4-5] (Figure 1). Without minimizing the time attributable to the structure of the healthcare system as such, it appears essential to reduce the time between the onset of the first disease-related symptoms and the first mention of these symptoms by the patient to a doctor (patient delay).

The question of patient delay has been extensively studied over the past few years. On the whole, these studies indicate that in Europe, for all cancers combined, the median delay between the onset of the first symptoms and the consultation for medical advice is three weeks [5]. However, the median delay by patients with head and neck cancers appears longer, varying between 3 and 9 weeks depending on the study and the location of the primary tumor [6-7]. This longer delay among these patients can be partially explained by the impact of socio-demographic, socio-economic, socio-educational and socio-cultural factors such as gender, age, socio-professional category, or the level of income or education [3, 8-11]. Other studies also emphasize the influence of psycho-social and behavioral differences with regard to smoking and alcohol consumption [12]. Nevertheless, these well-known factors do not seem to explain entirely the delay before consulting for these types of cancer; further clarification may be provided by a number of socio-cognitive and emotional factors.

In some diseases, for example, it has been shown that delayed consultation may be related to the patients becoming aware of their symptoms, how they assess these symptoms, their emotional impact [13-15], and the coping strategies implemented to deal with them [8,16-17]. The subject's social and family environment and the social support received also appear to be decisive factors [18-20]. More generally, based on the results of explanatory models used to analyze the factors influencing health behavior [21-25], the decision to consult a doctor after the onset of the first symptoms appears to be determined by the following:

- the patient's beliefs and perception of cancer, their feelings of vulnerability in the face of disease and their assessment of the seriousness of the perceived symptoms [21];
- the patient's perception of treatment and, more specifically, its benefits, as well as the perceived cost of consulting a specialist and the treatments liable to be prescribed [22];
- how the patient perceives their capacity to explain their symptoms to a doctor and consequently to take part in a treatment protocol and submit themselves to medical prescriptions [23-24];
- social incitation to consult a doctor (from the patient's relatives and the healthcare system) and the patient's acceptance of being influenced by the incitation of others [21-22];
- the emotions produced by the onset of the symptoms, the emotion regulation strategies implemented to cope with the situation, the difficulties experienced in doing so and any potential social support received [25];
- outside structural or environmental constraints and the subjective priority granted by the patient to resolve situational difficulties caused by changes in living conditions (loss of revenue, vulnerable family structure, financial insecurity, geographic distance from the healthcare centre, etc.) [23].

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This study aims to identify the factors explaining delayed consultation for head and neck cancers in the North of France (Nord-Pas de Calais region), where such cancers are particularly prevalent. Understanding which factors mostly determine the behavior of consulting a doctor when the first cancer symptoms appear seems to be essential for the adjustment and optimization of preventive messages in public health. In this context, the use of theoretical health decision models seems particularly suitable to approach this question of consultation delay from a global perspective. In order to modify patient health behavior, thus improving their vital prognosis and quality of life as well as reducing social inequalities regarding health, it seems essential to take into account not only patient representations concerning health but also the social, emotional and contextual determinants of their decisions and behavior.

This study aims to reveal the socio-cognitive and emotional factors associated with delayed consultation of a doctor following the onset of the first symptoms of cancer (patient delay). More precisely, the goal is to determine whether patient delay is related to (1) subjective perceptions concerning health, the disease, means of treatment, the healthcare system, the patient's capacity for action and self-efficiency, (2) emotion regulation strategies and difficulties, (3) the perceptions and behavior of the patient's relatives with regard to healthcare and prevention, (4) the information received and its sources, and (5) other situational difficulties.

The secondary objectives of the study are (1) to identify which medical, socio-demographic, socio-economic, socio-professional, socio-educational and geographic variables are related to delayed consultation of a doctor following the onset of the first symptoms, and (2) to ascertain the sources (attributable to the patient, the doctor, or the healthcare system) that most delay the final diagnosis of the disease and to determine which variables among those cited above

are associated with these sources of delay based on how the patients were managed medically between the onset of the first symptoms and diagnosis.

## Methods/design

The study is designed as interventional and does not involve products mentioned in article L.5311-1 of the French Code of Public Health. Participation in the study does not imply any changes in the medical care received by the patients.

#### **Population**

To be included in the study, patients must be over eighteen and have a cancer of the oral cavity (tongue, floor of the mouth, gums, palate and inside of the cheeks), of the oropharynx (tonsils, root of the tongue and soft palate), or of the hypopharynx and larynx (supra-glottis, glottis and sub-glottis). Only untreated patients will be invited to participate in the study, before any cognitive reappraisal of the situation induced by surgery, radiation therapy or medicinal treatment. Patients must be aware of their cancer diagnosis, understand and speak French fluently, and sign an informed consent to participate in the study. Exclusion criteria are cancer antecedents or psychiatric disorders liable to alter the patient's reasoning, discerning or judgmental abilities.

The "interview" sub-group will comprise patients who comply with all the above-mentioned selection criteria, who present no speech impediments and who agree to their comments being recorded.

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#### Number of patients and sample representativeness

The representativeness of our sample on a national scale will be ensured by patient recruitment in the main institutions responsible for treating head and neck cancers in the North of France (Nord-Pas-de-Calais region) where the incidence of this disease is particularly high. Patients treated in these centers come from the four large areas of the region with very different socio-cultural histories, which implies considerable socio-demographic and socio-professional diversity: the Lille metropolis (Oscar Lambret Center, Lille Regional University Hospital Centre, La Louvière private hospital), the coastal area (Coastal Specialized Medical Centre, Boulogne-sur-Mer Hospital Centre), the mining area (Lens Hospital Center) and Avesnois (patients mostly taken care of in the Lille metropolis). Sample representativeness will also be ensured by the participation of both state-run and private hospitals.

Given the nature of the investigation, it is not possible to calculate the number of participants required for the study. This will therefore be determined according to the feasibility of the study. The annual incidence of head and neck cancers in the Nord-Pas-de-Calais region is 4,000. This multicenter study will be performed in several hospitals which manage approximately 90% of patients with such cancers in the region. The sample will be composed of 400 patients in total, comprising 200 with early consultation and 200 with delayed consultation.

For the "interview" sub-sample, the answers given to an open question during semi-directive interviews often become redundant after around twenty participants. In order to enable a statistical comparison of the two groups of patients (early versus delayed consultation) and in view of the fact that the patients can only be separated into the two groups after all the data have been collected, the sub-sample has been enlarged to include 80 participants per group.

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This will enable statistical inference while preserving the feasibility of the study in terms of data analysis, since qualitative analysis of semi-directive interviews is particularly time-consuming.

#### Assessment criteria

#### 1 Main assessment criterion

The main assessment criterion is the time, in weeks, between the onset of the first cancerrelated symptoms and the first time the patient makes an appointment to see a doctor about these symptoms. This patient delay will be estimated based on three different reports to optimize data validity:

- 1) what the patient reports to the investigator (investigator's delay assessment),
- what the patient reports to the clinical research associate during completion of the face-to-face questionnaire (patient's delay assessment),
- 3) what the doctor who first saw the patient reports: the general practitioner or specialist will be contacted by phone after obtaining the patient's agreement (general practitioner's or private practice specialist's delay assessment).

#### 2 Secondary assessment criteria

The secondary assessment criteria concern the patient's medical data and socio-demographic, socio-economic, socio-educational and geographic indicators, as well as socio-cognitive and emotional indicators. The assessments will be made by: (1) completion of a case report form (CRF), (2) completion of a face-to-face questionnaire by a clinical research associate with the patient, (3) completion of a self-assessment questionnaire by the patient, and (4) the carrying out of a semi-directive interview with the patient by a competent psychologist mandated by the sponsor:

- case report form: primary location of the cancer, TNM classification at the stage of initial diagnosis, history of main medical and surgical events, current symptoms and treatments, treatment dates and modalities since the patient entered the treatment process;
- face-to-face questionnaire: socio-demographic, socio-professional, socio-economic and socio-educational indicators (gender, age, place of residence, lifestyle, professional activity, annual revenue, last diploma obtained, family history of chronic diseases), current symptoms and date of onset;
- self-assessment questionnaire: socio-cognitive and emotional determinants of the medical appointment that resulted in the detection of cancer (subjective perceptions concerning health, the first symptoms of the disease and treatments, feeling of control, emotional state, emotion regulation difficulties and strategies, social incitation, sources of medical information);
- 4) semi-directive interview only for patients in the "interview" sub-sample: determinants of the medical appointment that resulted in the patient taking part in an anti-cancer treatment protocol, specifically, on the one hand, subjective perceptions concerning the symptoms and the medical appointment, and on the other hand, subjective perceptions of health, the disease and treatments.

#### **Study conduct**

All the patients complying with all the selection criteria will be included in the study. Eligibility forms will be filled in by the investigator to ensure that the patient complies with all the selection criteria. The investigator will suggest the study to the patient and, if the latter agrees, the investigator will give the patient the information letter and ask them to sign the informed consent form. The patient will then be given an identification number corresponding

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to their chronological order of inclusion in the investigator's center. The eligibility form with the patient's identification number will be sent to the study sponsor so that their inclusion may be recorded. The clinical research associate will be in charge of filling in the CRF for the study. For

patients who are not in the "interview" sub-sample, an appointment will be made with a clinical research associate. He/she will fill in the face-to-face questionnaire with the patient. After that, the patient will fill in the self-assessment questionnaire. With the patient's agreement, the sponsor might re-contact them or their general practitioner at a later date to obtain any data that might be missing from the CRF or the face-to-face questionnaire.

For patients in the "interview" sub-sample, a first appointment will be made with a psychologist who will conduct the semi-directive interview which will be recorded (using a digital recorder) in compliance with the standardized procedure. Then, the patient will meet the clinical research associate for the face-to-face questionnaire and the self-assessment questionnaire.

In order not to constrain patients, appointments will always be planned for when patients are hospitalized (generally for complementary examinations), between the cancer diagnosis announcement and the beginning of treatment. The visit will take place in the patient's hospital room.

#### Analyses

Once the patient selection criteria have been checked, the statistical analyses will be performed by the URECA EA 1059 and EQUIPPE EA 4018 Research Units of Lille 3 University.

a) Quantitative analyses

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The geographic, socio-demographic, socio-professional, socio-economic, socio-educational, socio-cognitive, emotional and medical data will be presented in recapitulative or contingency tables summarizing the typical parameters used in descriptive statistics (frequencies, percentages, means, standard deviations depending on whether the variables are categorical or continuous). Contingency tables may be established for the different variables and targets if justified. Intergroup comparisons will be performed on this quantitative data using common parametric inferential statistics (ANOVA, MANOVA, Student's t-test) and non-parametric statistics (Chi-square, rank tests) to determine the differences, based on the different variables, between patients who consulted a doctor early versus those who consulted at a later stage after the onset of the first symptoms.

Ultimately, duration models (including the Cox model [26]) will be used to identify the causal and explanatory factors for delayed consultation. The results of the estimates will then be used for the implementation of preventive actions aimed at reducing delays. From a technical perspective, in order to obtain robust results, it will also be possible to check for potential assessment errors in the recording of consultation delays. Error measurement can be interesting for retrospective data collection based on the patients remembering events that might have occurred a long time beforehand. Tests are available to determine whether the assessment error is significant or not [27] and customized models may be applied to take into account any such potential assessment errors [28].

b) Qualitative analysis

The semi-directive interviews of the patients from the "interview" sub-sample will be analyzed qualitatively to identify the factors leading to the first medical consultation that resulted in the patient taking part in a treatment protocol. This step will be applied to all the interviews, regardless of the time taken by patients to consult their doctor. When all the

determinants of the medical consultation have been identified, the data will be synthesized by grouping the factors into categories. Descriptive and inferential quantitative analyses will then be performed for each of the two groups of patients (early versus late consultation) in order to compare how frequently the various factors were mentioned in the two groups to determine the factors associated with early consultation versus those associated with late consultation. Correlations between these data and the quantitative assessments obtained from the patients will be examined to show the links between the various determinants and medical consultation.

## Discussion

#### **Expected outcomes**

The data collected in this study will be used to evaluate the medical, geographic, sociodemographic, socio-professional, socio-economic, socio-educational, socio-cognitive and emotional factors affecting the consultation timeline after the onset of the first symptoms of head and neck cancers. This will help reveal the factors responsible for late diagnosis of patients suffering from these cancers. Given that the study considers medical, social, cognitive and emotional factors, it will confirm or invalidate the observations reported in the literature. Furthermore, it will enable the issue of late diagnosis to be addressed taking into account the full variety of factors affecting health behavior as they have been considered, often separately, in various theoretical models assessing health psychology. Based on these new observations, an index will be established assembling the most discriminatory variables affecting the populations at risk of consulting a doctor belatedly after the onset of the first cancer-related symptoms. This index, to be filled in systematically by patients (consulting in hospitals or with private practitioners), will contribute to a better understanding of delayed consultation

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for head and neck cancers. Fundamentally, the data collected in the study will enable the testing and adjustment of health decision models. The understanding of the factors affecting health-related behavior will be improved, as will the methods used to prevent pathogenic behavior and promote protective behavior.

#### **Potential impacts**

During this study, the identification of new determinants explaining delayed consultation will enable a better targeting of the populations at risk of entering a treatment protocol at a late stage. The results of this study will improve the determination of individual and group factors that may explain patient delay in consulting for medical advice, an essential parameter in the prevention of abnormally high death rates and social inequality with regard to access to healthcare for patients with head and neck cancers. Knowledge of the socio-economic environment of the patient's living place, combined with individual socio-economic information, will enable the influence of the context on patient delay to be analyzed.

However, it seems premature to design interventional studies straightaway, before the factors that are crucial and necessary for the formalization and setting up of such studies have been identified. The interests of specific health education systems, personalized screening, and healthcare interventions targeting populations at risk of delayed screening are undeniable. Depending on the results of this study, the populations considered at risk may, for example, be offered personalized psychosocial support, access to useful information to help them take health-related decisions, or easier access to the healthcare system and health-promoting systems. In addition, means may be implemented to increase the perceived capacity for action of at risk populations and their feelings of self-efficiency in terms of health.

The purpose of such operations would be to reduce diagnosis timelines in patients presenting with symptoms suggestive of head and neck cancers, with a view to (1) reducing the

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abnormally high death rates and changes in quality of life induced by delayed treatment and (2) fighting social inequality in terms of healthcare, a central component of the French Cancer Plan.



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The authors declare that they have no competing interests.

## **Author details**

VC, TL, MC, JF, and JLL contributed to the development and design of the protocol. CD and FV drafted the manuscript with critical input from all other authors who have read and approved the final manuscript.

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## 1 Abstract

**Introduction:** Reducing the time between the onset of the first symptoms of cancer and the first consultation with a doctor (patient delay) is essential to improve the vital prognosis and quality of life of patients. Longer patient delay is linked to already known socio-demographic, socio-economic, socio-educational, socio-cultural, and socio-professional factors. However, recent data suggest that some socio-cognitive and emotional determinants may explain patient delay from a complementary point of view. The main objective of this study is to assess whether, in head and neck cancer, patient delay is linked to these socio-cognitive and emotional factors, in addition to previously known factors.

Methods and Analysis: We intend to include in this study 400 patients with a not yet treated head and neck cancer diagnosed in one of six health centers in the North of France region. The main evaluation criterion is "patient delay". Socio-cognitive, emotional, medical, socio-demographic, socio-economic, educational, professional and geographic factors will be assessed by means of (1) a case report form, (2) a questionnaire completed by the clinical research associate together with the patient, (3) a questionnaire completed by the patient, and (4) a recorded semi-directive interview of the patient by a psychologist (for 80 patients only). The collected data will be analyzed to underline the differences between patients who consulted a doctor earlier versus those who consulted later.

19 Ethics: The study has obtained all the relevant authorizations for the protection of patients 20 enrolled in clinical trials (CCTIRS, CCP, CNIL), does not involve products mentioned in 21 article L.5311-1 of the French Code of Public Health, and does not imply any changes in the 22 medical care received by the patients. The study began in October 2012 and will end in June 23 2015. Trial registration: ID-RCB 2012-A00005-38

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### 1 Background

The time between the onset of the first symptoms and the effective treatment of patients with cancer seems to be a decisive factor in the vital prognosis of patients [1-2] and in the psychological adjustment of patients and their relatives [3]. In fact, the different intervals composing this delay (patient, primary care and secondary care intervals) have direct consequences on the tumor stage at the diagnosis and on short-term survival [4]. Therefore, reducing mortality related to avoidable cancers implies reducing the timeline between the initial diagnosis of the disease and the beginning of medical treatment. In addition to the time required for the prescription of medical examinations, the carrying out of examinations, the diagnosis of cancer, and treatment initiation, the delay between the onset of the first symptoms and the patient's consultation with a doctor seems to be a decisive factor in survival and quality of life [5-6] (Figure 1, [7]). Without minimizing the time attributable to the structure of the healthcare system as such, it appears essential to reduce the time between the onset of the first disease-related symptoms and the first mention of these symptoms by the patient to a doctor (patient delay).

The question of patient delay has been extensively studied over the past few years. A study conducted in Denmark shows that for all cancers combined the median delay between the onset of the first symptoms and the consultation for medical advice is three weeks [6]. Based on studies carried out in Scotland and England [8-9], the median delay for patients with head and neck cancers is around 30 days and appears longer than for other tumor locations. More precisely, head and neck cancer patients show the longest delay among 13 cancers [8] and oropharyngeal cancer patients show the longest delay among 18 cancers [9]. This longer delay among these patients can be partially explained by the impact of socio-demographic, socio-economic, socio-educational and socio-cultural factors such as gender, age, socio-professional category, or the level of income or education [3, 10-13]. Other studies also emphasize the

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influence of psychosocial and behavioral differences with regard to smoking and alcohol
consumption [14]. Nevertheless, these well-known factors do not seem to explain entirely the
delay before consulting for these types of cancer; further clarification may be provided by a
number of socio-cognitive and emotional factors.

In some diseases, for example, it has been shown that delayed consultation may be related to the patients becoming aware of their symptoms, how they assess these symptoms, their emotional impact [15-17], and the coping strategies implemented to deal with them [10,18-19]. The subject's social and family environment and the social support received also appear to be decisive factors [20-22]. These components have been underlined by the model of Pathways to Treatment and empirical data [23-24], which distinguish between the appraisal interval ("the time from the detection of a bodily change to perceiving a reason to discuss symptoms with a HCP [Health Care Provider]" and the help-seeking interval ("the time from perceiving a reason to discuss symptoms with a HCP to the first consultation with a HCP about their symptoms") [23]. The main determinants identified in the literature cover these different steps from the perception and interpretation of the symptoms (e.g. gravity), to emotional regulation and coping (e.g. avoidance), then to the perception of a reason to consult a doctor and the decision to consult him/her actually (e.g. perceived costs and benefits, self-efficacy and outcome expectations) [23]. More generally, based on the results of explanatory models used to analyze the factors influencing health behavior [25-30], the decision to consult a doctor after the onset of the first symptoms appears to be determined by the following:

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Subjective perceptions concerning health: the patient's beliefs and perception of
 cancer [31-32], feelings of vulnerability in relation to the disease, assessment of the
 gravity of the perceived symptoms [25], as well as reappraisal of some warning signs
 of cancer [33], which is particularly relevant for head and neck cancers as some
 symptoms are common and may be misattributed [23];

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Perception of medical care: the patient's perception of treatments and, more specifically, benefits, or on the contrary fatalism regarding cancer [34]; perceived barriers to the seeking of medical advice [35-37], especially how patients perceive their capacity to explain their symptoms to a doctor and consequently to take part in a treatment protocol and submit themselves to medical prescriptions [26-27];

- Social incitation to consult a doctor: from the patient's relatives and the healthcare system; the patient's acceptance of being influenced by the incitation of others [25, 28];
- *Emotional factors*: the emotions produced by the onset of the symptoms, emotion regulation strategies implemented to cope with the situation, difficulties experienced in doing so and any potential social support received [29];
- Structural or environmental constraints: the subjective priority granted by the patient
   to resolve situational difficulties caused by changes in living conditions (loss of
   revenue, vulnerable family structure, financial insecurity, geographic distance from
   the healthcare centre, etc.) [27,38].

This study aims to identify the factors explaining delayed consultation for head and neck cancers in the North of France (Nord-Pas de Calais region), where such cancers are particularly prevalent. Understanding which factors mostly determine the behavior of consulting a doctor when the first cancer symptoms appear seems to be essential for the adjustment and optimization of preventive messages in public health. In this context, the use of theoretical health decision models seems particularly suitable to approach this question of consultation delay from a global perspective. In order to modify patient health behavior, thus improving their vital prognosis and quality of life as well as reducing social inequalities regarding health, it seems essential to take into account not only patient representations

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concerning health but also the social, emotional and contextual determinants of their decisions and behavior.

This study aims to reveal the socio-cognitive and emotional factors associated with delayed consultation of a doctor following the onset of the first symptoms of cancer (patient delay). More precisely, the goal is to determine whether patient delay is related to (1) subjective perceptions concerning health, the disease, means of treatment, the healthcare system, the patient's capacity for action and self-efficiency, (2) emotion regulation strategies and difficulties, (3) the perceptions and behavior of the patient's relatives with regard to healthcare and prevention, (4) the information received and its sources, and (5) other situational difficulties.

The secondary objectives of the study are (1) to identify which medical, socio-demographic, socio-economic, socio-professional, socio-educational and geographic variables are related to delayed consultation of a doctor following the onset of the first symptoms, and (2) to ascertain the sources (attributable to the patient, the doctor, or the healthcare system) that most delay the final diagnosis of the disease and to determine which variables among those cited above are associated with these sources of delay based on how the patients were managed medically between the onset of the first symptoms and diagnosis.

#### Methods/design

The study has obtained all the relevant authorizations for the protection of patients enrolled in clinical trials (CCTIRS, CCP, CNIL), does not involve products mentioned in article L.5311-1 of the French Code of Public Health, and does not imply any changes in the medical care received by the patients. The study began in October 2012 and will end in June 2015.

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To be included in the study, patients must be over eighteen and have a cancer of the oral cavity (tongue, floor of the mouth, gums, palate and inside of the cheeks), of the oropharynx (tonsils, root of the tongue and soft palate), or of the hypopharynx and larvnx (supra-glottis, glottis and sub-glottis). Only untreated patients will be invited to participate in the study, before any cognitive reappraisal of the situation induced by surgery, radiation therapy or medicinal treatment. Patients must be aware of their cancer diagnosis, understand and speak French fluently, and sign an informed consent to participate in the study. Exclusion criteria are cancer antecedents or psychiatric disorders liable to alter the patient's reasoning, discerning or judgmental abilities.

11 The "interview" sub-group will comprise patients who comply with all the above-mentioned 12 selection criteria, who present no speech impediments and who agree to their comments being 13 recorded.

#### 14 Number of patients and sample representativeness

The representativeness of our sample on a national scale will be ensured by patient recruitment in the main institutions responsible for treating head and neck cancers in the North of France (Nord-Pas-de-Calais region) where the incidence of this disease is particularly high. Patients treated in these centers come from the four large areas of the region with very different socio-cultural histories, which implies considerable socio-demographic and socio-professional diversity: the Lille metropolis (Oscar Lambret Center, Lille Regional University Hospital Centre, La Louvière private hospital), the coastal area (Coastal Specialized Medical Centre, Boulogne-sur-Mer Hospital Centre), the mining area (Lens Hospital Center) and Avesnois (patients mostly taken care of in the Lille metropolis). Sample

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representativeness will also be ensured by the participation of both state-run and private hospitals.

Given the nature of the investigation, it is not possible to calculate the number of participants required for the study. This will therefore be determined according to the feasibility of the study. The annual incidence of head and neck cancers in the Nord-Pas-de-Calais region is 4,000. This multicenter study will be performed in several hospitals which manage approximately 90% of patients with such cancers in the region. The sample will be composed of 400 patients in total, comprising 200 with early consultation and 200 with delayed consultation.

For the "interview" sub-sample, the answers given to an open question during semi-directive interviews often become redundant after around twenty participants. In order to enable a statistical comparison of the two groups of patients (early versus delayed consultation) and in view of the fact that the patients can only be separated into the two groups after all the data have been collected, the sub-sample has been enlarged to include 80 participants per group. This will enable statistical inference while preserving the feasibility of the study in terms of data analysis, since qualitative analysis of semi-directive interviews is particularly time-consuming.

### 18 Assessment criteria

#### 19 1 Main assessment criterion

The main assessment criterion is the time, in weeks, between the onset of the first cancerrelated symptoms and the first time the patient makes an appointment to talk to a doctor about these symptoms. This patient delay will be estimated based on three different reports to optimize data validity:

1) what the patient reports to the investigator (patient delay reported by the investigator), 2) what the patient reports to the clinical research associate during completion of the face-to-face questionnaire (patient delay reported by the clinical research associate), 3) what the doctor who first saw the patient reports: the general practitioner or specialist will be contacted by phone after obtaining the patient's agreement (patient delay reported by the general practitioner or private practice specialist). Secondary assessment criteria The secondary assessment criteria concern the patient's medical data and socio-demographic, socio-economic, socio-educational and geographic indicators, as well as socio-cognitive and emotional indicators. The assessments will be made by: (1) completion of a case report form (CRF), (2) completion of a face-to-face questionnaire by a clinical research associate with the patient, (3) completion of a self-assessment questionnaire by the patient, and (4) the carrying

16 the sponsor:

 Case report form: primary location of the cancer, TNM classification at the stage of initial diagnosis, history of main medical and surgical events, current symptoms and treatments, treatment dates and modalities since the patient entered the treatment process;

out of a semi-directive interview with the patient by a competent psychologist mandated by

2) Face-to-face questionnaire: socio-demographic, socio-professional, socio-economic and socio-educational indicators (gender, age, place of residence, lifestyle, professional activity, annual revenue, last diploma obtained, family history of chronic diseases), usual health behaviors (frequency of consultations, tobacco and alcohol

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2 3	1	consumption), current symptoms (presence or not, duration, and perceived link with
4 5 6	2	cancer from the patient's point of view) and date of the onset;
6 7 8	3	3) Self-assessment questionnaire: socio-cognitive and emotional determinants of the
9 10	4	medical appointment that resulted in the detection of cancer. Based on theoretical
11 12	5	models, items – 7-point Likert scales – have been specifically built with a view to
13 14	6	understanding delay determinants:
15 16	7	a Subjective neurontions concerning health importance given to health and
17 18	/	o subjective perceptions concerning nearth, importance given to hearth and
19	8	perceived vulnerability to diseases before the onset of the first symptoms (3
20 21 22	9	items); first symptoms of the disease: perceived gravity and anxiety in relation
22 23 24	10	to the symptoms (2 items);
24 25 26	11	• <i>Perception of medical care:</i> feeling of control regarding a possible treatment:
27 28	12	perceived costs, perceived benefits and self-efficacy (5 items);
29 30	13	• Social incitation to consult: incitation from relatives and value given to this
31 32	14	incitation (2 items); sources of medical information: relatives, media,
33 34 25	15	pharmacist (3 items);
36 37	16	• Emotional factors: emotional state: anxiety and depression moods (4 items);
38 39	17	emotion regulation difficulties and strategies: difficulty in cooling down -
40 41	18	emotion regulation strategies (avoidance, reappraisal, social sharing of
42 43 44	19	emotions, symptom-centered coping) (5 items);
45 46	20	• Structural or environmental constraints: health may not be a priority, patient
47 48	21	faced with other practical difficulties (2 items).
49 50	22	4) Semi-directive interview only for patients in the "interview" sub-sample:
51 52	23	determinants of the medical appointment that resulted in the patient taking part in an
53 54 55 56	24	anti-cancer treatment protocol, specifically, on the one hand, subjective perceptions
57 58 59		

concerning the symptoms and the medical appointment, and on the other hand, subjective perceptions of health, the disease and treatments.

#### **Study conduct**

All the patients complying with all the selection criteria will be included in the study. Eligibility forms will be filled in by the investigator to ensure that the patient complies with all the selection criteria. The investigator will suggest the study to the patient and, if the latter agrees, the investigator will give the patient the information letter and ask them to sign the informed consent form. The patient will then be given an identification number corresponding to their chronological order of inclusion in the investigator's center. The eligibility form with the patient's identification number will be sent to the study sponsor so that their inclusion may be recorded.

The clinical research associate will be in charge of filling in the CRF for the study. For patients who are not in the "interview" sub-sample, an appointment will be made with a clinical research associate. He/she will fill in the face-to-face questionnaire with the patient. After that, the patient will fill in the self-assessment questionnaire. With the patient's agreement, the sponsor might re-contact them or their general practitioner at a later date to obtain any data that might be missing from the CRF or the face-to-face questionnaire.

For patients in the "interview" sub-sample, a first appointment will be made with a psychologist who will conduct the semi-directive interview which will be recorded (using a digital recorder) in compliance with the standardized procedure. Then, the patient will meet the clinical research associate for the face-to-face questionnaire and the self-assessment questionnaire.
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In order not to constrain patients, appointments will always be planned for when patients are hospitalized (generally for complementary examinations), between the cancer diagnosis announcement and the beginning of treatment. The visit will take place in the patient's hospital room.

## 5 Analyses

Once the patient selection criteria have been checked, the statistical analyses will be
performed by the URECA EA 1059 and EQUIPPE EA 4018 Research Units of Lille 3
University.

a) Quantitative analyses

The geographic, socio-demographic, socio-professional, socio-economic, socio-educational, socio-cognitive, emotional and medical data will be presented in recapitulative or contingency tables summarizing the typical parameters used in descriptive statistics (frequencies, percentages, means, standard deviations depending on whether the variables are categorical or continuous). Contingency tables may be established for the different variables and targets if justified. Intergroup comparisons will be performed on this quantitative data using common parametric inferential statistics (ANOVA, MANOVA, Student's t-test) and non-parametric statistics (Chi-square, rank tests) to determine the differences, based on the different variables, between patients who consulted a doctor early versus those who consulted at a later stage after the onset of the first symptoms. Early versus late consultation groups will be defined on the basis of the median of the averages of the three measures of delay (patient delay reported by the investigator, by the clinical research associate, and by the general practitioner or private practice specialist).

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Ultimately, duration models (including the Cox model [39]) will be used to identify the causal and explanatory factors for delayed consultation. The results of the estimates will then be used for the implementation of preventive actions aimed at reducing delays. From a technical perspective, in order to obtain robust results, it will also be possible to check for potential assessment errors in the recording of consultation delays. Error measurement can be interesting for retrospective data collection based on the patients remembering events that might have occurred a long time beforehand. Tests are available to determine whether the assessment error is significant or not [40] and customized models may be applied to take into account any such potential assessment errors [41]. b) Qualitative analysis 

The semi-directive interviews of the patients from the "interview" sub-sample will be analyzed qualitatively to identify the factors leading to the first medical consultation that resulted in the patient taking part in a treatment protocol. This step will be applied to all the interviews, regardless of the time taken by patients to consult their doctor. When all the determinants of the medical consultation have been identified, the data will be synthesized by grouping the factors into categories. Descriptive and inferential quantitative analyses will then be performed for each of the two groups of patients (early versus late consultation) in order to compare how frequently the various factors were mentioned in the two groups to determine the factors associated with early consultation versus those associated with late consultation. Correlations between these data and the quantitative assessments obtained from the patients will be examined to show the links between the various determinants and medical consultation.

# Discussion

# **Expected outcomes**

The data collected in this study will be used to evaluate the medical, geographic, socio-demographic, socio-professional, socio-economic, socio-educational, socio-cognitive and emotional factors affecting the consultation timeline after the onset of the first symptoms of head and neck cancers. This will help reveal the factors responsible for late diagnosis of patients suffering from these cancers. Given that the study considers medical, social, cognitive and emotional factors, it will confirm or invalidate the observations reported in the literature. Moreover, the results about psychosocial determinants will be analyzed and discussed to gain a broader theoretical understanding of the processes of deciding to consult (appraisal and help-seeking interval, [23]) in order to identify the appropriate level to offer intervention and/or further investigations. Furthermore, it will enable the issue of late diagnosis to be addressed taking into account the full variety of factors affecting health behavior as they have been considered, often separately, in various theoretical models assessing health psychology. Based on these new observations, an index will be established assembling the most discriminatory variables affecting populations at risk of consulting a doctor belatedly after the onset of the first cancer-related symptoms. Fundamentally, the data collected in the study will enable the testing and adjustment of health decision models. The understanding of the factors affecting health-related behavior will be improved, as will the methods used to prevent pathogenic behavior and promote protective behavior.

# 21 Strengths and limitations of the design

22 Because this design strives to understand the many determinants of delay and has important 23 implications for the literature as well as for implementing interventions, it is important to

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summarize its strengths and point out its limitations, inspired in part by the Aarhus checklist [42]. First, the beginning and the end points of the consultation delay are clearly defined and their assessment is therefore replicable. As the recall of the onset of symptoms may involve some recall biases, three measurements with different methods will be used to minimize the measurement error. Moreover, the self-assessment questionnaire including socio-cognitive and emotional determinants has been built to assess the specific hypotheses of this study. We have made this choice because 1) given the large range of variables studied, the use of specific validated questionnaires assessing each variable would be impossible, 2) some questionnaires (e.g. the importance of health in patients' personal priorities, their perceptions and reactions when they are faced with the onset of the first symptoms) do not exist, or have not yet been validated, or are difficult to find and 3) we have taken many precautions to build the scales on the basis of relevant and up-to-date theoretical models, inspired from previous studies, and the relevance and wording of items have been discussed carefully with several researchers involved in the care of head and neck cancer patients. We are convinced that all these methodological precautions will ensure the reliability of the data collected in this study.

# **Potential impacts**

During this study, the identification of new determinants explaining delayed consultation will enable a better targeting of the populations at risk of entering a treatment protocol at a late stage. The results of this study will improve the determination of individual and group factors that may explain patient delay in consulting for medical advice, an essential parameter in the prevention of abnormally high death rates and social inequality with regard to access to healthcare for patients with head and neck cancers. Knowledge of the socio-economic environment of the patient's living place, combined with individual socio-economic information, will enable the influence of the context on patient delay to be analyzed.

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However, it seems premature to design interventional studies straightaway, before the factors that are crucial and necessary for the formalization and setting up of such studies have been identified. The interests of specific health education systems, personalized screening, and healthcare interventions targeting populations at risk of delayed screening are undeniable. Depending on the results of this study, the populations considered at risk may, for example, be offered personalized psychosocial support, access to useful information to help them take health-related decisions, or easier access to the healthcare system and health-promoting systems. In addition, means may be implemented to increase the perceived capacity for action of at risk populations and their feelings of self-efficiency in terms of health.

10 The purpose of such operations would be to reduce diagnosis timelines in patients presenting 11 with symptoms suggestive of head and neck cancers, with a view to (1) reducing the 12 abnormally high death rates and changes in quality of life induced by delayed treatment and 13 (2) fighting social inequality in terms of healthcare, a central component of the French Cancer 14 Plan.

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# 4 Competing interests

5 The authors declare that they have no competing interests.

# 6 Author details

VC, TL, MC, JF, and JLL contributed to the development and design of the protocol. CD and
FV drafted the manuscript with critical input from all other authors who have read and
approved the final manuscript.

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#### **Figure legend**

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# Determinants of patient delay in doctor consultation in head and neck cancers (Protocol DEREDIA)

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# 1 Abstract

Introduction: Reducing the time between the onset of the first symptoms of cancer and the first consultation with a doctor (patient delay) is essential to improve the vital prognosis and quality of life of patients. Longer patient delay is linked to already known socio-demographic, socio-economic, socio-educational, socio-cultural, and socio-professional factors. However, recent data suggest that some socio-cognitive and emotional determinants may explain patient delay from a complementary point of view. The main objective of this study is to assess whether, in head and neck cancer, patient delay is linked to these socio-cognitive and emotional factors, in addition to previously known factors.

Methods and Analysis: We intend to include in this study 400 patients with a not yet treated head and neck cancer diagnosed in one of six health centers in the North of France region. The main evaluation criterion is "patient delay". Socio-cognitive, emotional, medical, socio-demographic, socio-economic, educational, professional and geographic factors will be assessed by means of (1) a case report form, (2) a questionnaire completed by the clinical research associate together with the patient, (3) a questionnaire completed by the patient, and (4) a recorded semi-directive interview of the patient by a psychologist (for 80 patients only). The collected data will be analyzed to underline the differences between patients who consulted a doctor earlier versus those who consulted later.

19 Ethics: The study has obtained all the relevant authorizations for the protection of patients 20 enrolled in clinical trials (CCTIRS, CCP, CNIL), does not involve products mentioned in 21 article L.5311-1 of the French Code of Public Health, and does not imply any changes in the 22 medical care received by the patients. The study began in October 2012 and will end in June 23 2015. Trial registration: ID-RCB 2012-A00005-38

# 1 Background

The time between the onset of the first symptoms and the effective treatment of patients with cancer seems to be a decisive factor in the vital prognosis of patients [1-2] and in the psychological adjustment of patients and their relatives [3]. In fact, the different intervals composing this delay (patient, primary care and secondary care intervals) have direct consequences on the tumor stage at the diagnosis and on short-term survival [4]. Therefore, reducing mortality related to avoidable cancers implies reducing the timeline between the initial diagnosis of the disease and the beginning of medical treatment. In addition to the time required for the prescription of medical examinations, the carrying out of examinations, the diagnosis of cancer, and treatment initiation, the delay between the onset of the first symptoms and the patient's consultation with a doctor seems to be a decisive factor in survival and quality of life [5-6] (Figure 1, [7]). Without minimizing the time attributable to the structure of the healthcare system as such, it appears essential to reduce the time between the onset of the first disease-related symptoms and the first mention of these symptoms by the patient to a doctor (patient delay).

The question of patient delay has been extensively studied over the past few years. A study conducted in Denmark shows that for all cancers combined the median delay between the onset of the first symptoms and the consultation for medical advice is three weeks [6]. Based on studies carried out in Scotland and England [8-9], the median delay for patients with head and neck cancers is around 30 days and appears longer than for other tumor locations. More precisely, head and neck cancer patients show the longest delay among 13 cancers [8] and oropharyngeal cancer patients show the longest delay among 18 cancers [9]. This longer delay among these patients can be partially explained by the impact of socio-demographic, socio-economic, socio-educational and socio-cultural factors such as gender, age, socio-professional category, or the level of income or education [3, 10-13]. Other studies also emphasize the

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influence of psychosocial and behavioral differences with regard to smoking and alcohol
consumption [14]. Nevertheless, these well-known factors do not seem to explain entirely the
delay before consulting for these types of cancer; further clarification may be provided by a
number of socio-cognitive and emotional factors.

In some diseases, for example, it has been shown that delayed consultation may be related to the patients becoming aware of their symptoms, how they assess these symptoms, their emotional impact [15-17], and the coping strategies implemented to deal with them [10,18-19]. The subject's social and family environment and the social support received also appear to be decisive factors [20-22]. These components have been underlined by the model of Pathways to Treatment and empirical data [23-24], which distinguish between the appraisal interval ("the time from the detection of a bodily change to perceiving a reason to discuss symptoms with a HCP [Health Care Provider]" and the help-seeking interval ("the time from perceiving a reason to discuss symptoms with a HCP to the first consultation with a HCP about their symptoms") [23]. The main determinants identified in the literature cover these different steps from the perception and interpretation of the symptoms (e.g. gravity), to emotional regulation and coping (e.g. avoidance), then to the perception of a reason to consult a doctor and the decision to consult him/her actually (e.g. perceived costs and benefits, self-efficacy and outcome expectations) [23]. More generally, based on the results of explanatory models used to analyze the factors influencing health behavior [25-30], the decision to consult a doctor after the onset of the first symptoms appears to be determined by the following:

Subjective perceptions concerning health: the patient's beliefs and perception of cancer [31-32], feelings of vulnerability in relation to the disease, assessment of the gravity of the perceived symptoms [25], as well as reappraisal of some warning signs of cancer [33], which is particularly relevant for head and neck cancers as some symptoms are common and may be misattributed [23];

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1	• Perception of medical care: the patient's perception of treatments and, more
2	specifically, benefits, or on the contrary fatalism regarding cancer [34]; perceived
3	barriers to the seeking of medical advice [35-37], especially how patients perceive
4	their capacity to explain their symptoms to a doctor and consequently to take part in a
5	treatment protocol and submit themselves to medical prescriptions [26-27];
6	• Social incitation to consult a doctor: from the patient's relatives and the healthcare
7	system; the patient's acceptance of being influenced by the incitation of others [25,
8	28];
9	• Emotional factors: the emotions produced by the onset of the symptoms, emotion
10	regulation strategies implemented to cope with the situation, difficulties experienced
11	in doing so and any potential social support received [29];
12	• Structural or environmental constraints: the subjective priority granted by the patient
13	to resolve situational difficulties caused by changes in living conditions (loss of
14	revenue, vulnerable family structure, financial insecurity, geographic distance from
15	the healthcare centre, etc.) [27,38].
16	This study aims to identify the factors explaining delayed consultation for head and neck
17	cancers in the North of France (Nord-Pas de Calais region), where such cancers are
18	particularly prevalent. Understanding which factors mostly determine the behavior of
19	consulting a doctor when the first cancer symptoms appear seems to be essential for the
20	adjustment and optimization of preventive messages in public health. In this context, the use
21	of theoretical health decision models seems particularly suitable to approach this question of
22	consultation delay from a global perspective. In order to modify patient health behavior, thus
23	improving their vital prognosis and quality of life as well as reducing social inequalities

24 regarding health, it seems essential to take into account not only patient representations

concerning health but also the social, emotional and contextual determinants of their decisions
 and behavior.

This study aims to reveal the socio-cognitive and emotional factors associated with delayed consultation of a doctor following the onset of the first symptoms of cancer (patient delay). More precisely, the goal is to determine whether patient delay is related to (1) subjective perceptions concerning health, the disease, means of treatment, the healthcare system, the patient's capacity for action and self-efficiency, (2) emotion regulation strategies and difficulties, (3) the perceptions and behavior of the patient's relatives with regard to healthcare and prevention, (4) the information received and its sources, and (5) other situational difficulties.

The secondary objectives of the study are (1) to identify which medical, socio-demographic, socio-economic, socio-professional, socio-educational and geographic variables are related to delayed consultation of a doctor following the onset of the first symptoms, and (2) to ascertain the sources (attributable to the patient, the doctor, or the healthcare system) that most delay the final diagnosis of the disease and to determine which variables among those cited above are associated with these sources of delay based on how the patients were managed medically between the onset of the first symptoms and diagnosis.

# 18 Methods/design

The study has obtained all the relevant authorizations for the protection of patients enrolled in
clinical trials (CCTIRS, CCP, CNIL), does not involve products mentioned in article L.53111 of the French Code of Public Health, and does not imply any changes in the medical care
received by the patients. The study began in October 2012 and will end in June 2015.

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# **Population**

To be included in the study, patients must be over eighteen and have a cancer of the oral cavity (tongue, floor of the mouth, gums, palate and inside of the cheeks), of the oropharynx (tonsils, root of the tongue and soft palate), or of the hypopharynx and larvnx (supra-glottis, glottis and sub-glottis). Only untreated patients will be invited to participate in the study, before any cognitive reappraisal of the situation induced by surgery, radiation therapy or medicinal treatment. Patients must be aware of their cancer diagnosis, understand and speak French fluently, and sign an informed consent to participate in the study. Exclusion criteria are cancer antecedents or psychiatric disorders liable to alter the patient's reasoning, discerning or judgmental abilities.

11 The "interview" sub-group will comprise patients who comply with all the above-mentioned 12 selection criteria, who present no speech impediments and who agree to their comments being 13 recorded.

# 14 Number of patients and sample representativeness

The representativeness of our sample on a national scale will be ensured by patient recruitment in the main institutions responsible for treating head and neck cancers in the North of France (Nord-Pas-de-Calais region) where the incidence of this disease is particularly high. Patients treated in these centers come from the four large areas of the region with very different socio-cultural histories, which implies considerable socio-demographic and socio-professional diversity: the Lille metropolis (Oscar Lambret Center, Lille Regional University Hospital Centre, La Louvière private hospital), the coastal area (Coastal Specialized Medical Centre, Boulogne-sur-Mer Hospital Centre), the mining area (Lens Hospital Center) and Avesnois (patients mostly taken care of in the Lille metropolis). Sample

representativeness will also be ensured by the participation of both state-run and private
 hospitals.

Given the nature of the investigation, it is not possible to calculate the number of participants required for the study. This will therefore be determined according to the feasibility of the study. The annual incidence of head and neck cancers in the Nord-Pas-de-Calais region is 4,000. This multicenter study will be performed in several hospitals which manage approximately 90% of patients with such cancers in the region. The sample will be composed of 400 patients in total, comprising 200 with early consultation and 200 with delayed consultation.

For the "interview" sub-sample, the answers given to an open question during semi-directive interviews often become redundant after around twenty participants. In order to enable a statistical comparison of the two groups of patients (early versus delayed consultation) and in view of the fact that the patients can only be separated into the two groups after all the data have been collected, the sub-sample has been enlarged to include 80 participants per group. This will enable statistical inference while preserving the feasibility of the study in terms of data analysis, since qualitative analysis of semi-directive interviews is particularly time-consuming.

# 18 Assessment criteria

## 19 1 Main assessment criterion

The main assessment criterion is the time, in weeks, between the onset of the first cancerrelated symptoms and the first time the patient makes an appointment to talk to a doctor about these symptoms. This patient delay will be estimated based on three different reports to optimize data validity:

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1) what the patient reports to the investigator (patient delay reported by the investigator),

2) what the patient reports to the clinical research associate during completion of the face-to-face questionnaire (patient delay reported by the clinical research associate),

3) what the doctor who first saw the patient reports: the general practitioner or specialist will be contacted by phone after obtaining the patient's agreement (patient delay reported by the general practitioner or private practice specialist).

2 Secondary assessment criteria

The secondary assessment criteria concern the patient's medical data and socio-demographic, socio-economic, socio-educational and geographic indicators, as well as socio-cognitive and emotional indicators. The assessments will be made by: (1) completion of a case report form (CRF), (2) completion of a face-to-face questionnaire by a clinical research associate with the patient, (3) completion of a self-assessment questionnaire by the patient, and (4) the carrying out of a semi-directive interview with the patient by a competent psychologist mandated by the sponsor: BMJ Open: first published as 10.1136/bmjopen-2014-005286 on 25 July 2014. Downloaded from http://bmjopen.bmj.com/ on June 7, 2025 at Department GEZ-LTA Erasmushogeschool .

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Case report form: primary location of the cancer, TNM classification at the stage of
 initial diagnosis, history of main medical and surgical events, current symptoms and
 treatments, treatment dates and modalities since the patient entered the treatment
 process;

2) Face-to-face questionnaire: socio-demographic, socio-professional, socio-economic and socio-educational indicators (gender, age, place of residence, lifestyle, professional activity, annual revenue, last diploma obtained, family history of chronic diseases), usual health behaviors (frequency of consultations, tobacco and alcohol

1	consumption), current symptoms (presence or not, duration, and perceived link with
2	cancer from the patient's point of view) and date of the onset;
3	3) Self-assessment questionnaire: socio-cognitive and emotional determinants of the
4	medical appointment that resulted in the detection of cancer. Based on theoretical
5	models, items - 7-point Likert scales - have been specifically built with a view to
6	understanding delay determinants:
7	• Subjective perceptions concerning health: importance given to health and
8	perceived vulnerability to diseases before the onset of the first symptoms (3
9	items); first symptoms of the disease: perceived gravity and anxiety in relation
10	to the symptoms (2 items);
11	• <i>Perception of medical care:</i> feeling of control regarding a possible treatment:
12	perceived costs, perceived benefits and self-efficacy (5 items);
13	• Social incitation to consult: incitation from relatives and value given to this
14	incitation (2 items); sources of medical information: relatives, media,
15	pharmacist (3 items);
16	• Emotional factors: emotional state: anxiety and depression moods (4 items);
17	emotion regulation difficulties and strategies: difficulty in cooling down -
18	emotion regulation strategies (avoidance, reappraisal, social sharing of
19	emotions, symptom-centered coping) (5 items);
20	• Structural or environmental constraints: health may not be a priority, patient
21	faced with other practical difficulties (2 items).
22	4) Semi-directive interview only for patients in the "interview" sub-sample:
23	determinants of the medical appointment that resulted in the patient taking part in an
24	anti-cancer treatment protocol, specifically, on the one hand, subjective perceptions

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concerning the symptoms and the medical appointment, and on the other hand, subjective perceptions of health, the disease and treatments.

# 3 Study conduct

All the patients complying with all the selection criteria will be included in the study. Eligibility forms will be filled in by the investigator to ensure that the patient complies with all the selection criteria. The investigator will suggest the study to the patient and, if the latter agrees, the investigator will give the patient the information letter and ask them to sign the informed consent form. The patient will then be given an identification number corresponding to their chronological order of inclusion in the investigator's center. The eligibility form with the patient's identification number will be sent to the study sponsor so that their inclusion may be recorded.

The clinical research associate will be in charge of filling in the CRF for the study. For patients who are not in the "interview" sub-sample, an appointment will be made with a clinical research associate. He/she will fill in the face-to-face questionnaire with the patient. After that, the patient will fill in the self-assessment questionnaire. With the patient's agreement, the sponsor might re-contact them or their general practitioner at a later date to obtain any data that might be missing from the CRF or the face-to-face questionnaire.

For patients in the "interview" sub-sample, a first appointment will be made with a psychologist who will conduct the semi-directive interview which will be recorded (using a digital recorder) in compliance with the standardized procedure. Then, the patient will meet the clinical research associate for the face-to-face questionnaire and the self-assessment questionnaire. In order not to constrain patients, appointments will always be planned for when patients are hospitalized (generally for complementary examinations), between the cancer diagnosis announcement and the beginning of treatment. The visit will take place in the patient's hospital room.

# 5 Analyses

Once the patient selection criteria have been checked, the statistical analyses will be
performed by the URECA EA 1059 and EQUIPPE EA 4018 Research Units of Lille 3
University.

a) Quantitative analyses

The geographic, socio-demographic, socio-professional, socio-economic, socio-educational, socio-cognitive, emotional and medical data will be presented in recapitulative or contingency tables summarizing the typical parameters used in descriptive statistics (frequencies, percentages, means, standard deviations depending on whether the variables are categorical or continuous). Contingency tables may be established for the different variables and targets if justified. Intergroup comparisons will be performed on this quantitative data using common parametric inferential statistics (ANOVA, MANOVA, Student's t-test) and non-parametric statistics (Chi-square, rank tests) to determine the differences, based on the different variables, between patients who consulted a doctor early versus those who consulted at a later stage after the onset of the first symptoms. Early versus late consultation groups will be defined on the basis of the median of the averages of the three measures of delay (patient delay reported by the investigator, by the clinical research associate, and by the general practitioner or private practice specialist).

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Ultimately, duration models (including the Cox model [39]) will be used to identify the causal and explanatory factors for delayed consultation. The results of the estimates will then be used for the implementation of preventive actions aimed at reducing delays. From a technical perspective, in order to obtain robust results, it will also be possible to check for potential assessment errors in the recording of consultation delays. Error measurement can be interesting for retrospective data collection based on the patients remembering events that might have occurred a long time beforehand. Tests are available to determine whether the assessment error is significant or not [40] and customized models may be applied to take into account any such potential assessment errors [41].

10 b) Qualitative analysis

The semi-directive interviews of the patients from the "interview" sub-sample will be analyzed qualitatively to identify the factors leading to the first medical consultation that resulted in the patient taking part in a treatment protocol. This step will be applied to all the interviews, regardless of the time taken by patients to consult their doctor. When all the determinants of the medical consultation have been identified, the data will be synthesized by grouping the factors into categories. Descriptive and inferential quantitative analyses will then be performed for each of the two groups of patients (early versus late consultation) in order to compare how frequently the various factors were mentioned in the two groups to determine the factors associated with early consultation versus those associated with late consultation. Correlations between these data and the quantitative assessments obtained from the patients will be examined to show the links between the various determinants and medical consultation.

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# 1 Discussion

# **Expected outcomes**

The data collected in this study will be used to evaluate the medical, geographic, socio-demographic, socio-professional, socio-economic, socio-educational, socio-cognitive and emotional factors affecting the consultation timeline after the onset of the first symptoms of head and neck cancers. This will help reveal the factors responsible for late diagnosis of patients suffering from these cancers. Given that the study considers medical, social, cognitive and emotional factors, it will confirm or invalidate the observations reported in the literature. Moreover, the results about psychosocial determinants will be analyzed and discussed to gain a broader theoretical understanding of the processes of deciding to consult (appraisal and help-seeking interval, [23]) in order to identify the appropriate level to offer intervention and/or further investigations. Furthermore, it will enable the issue of late diagnosis to be addressed taking into account the full variety of factors affecting health behavior as they have been considered, often separately, in various theoretical models assessing health psychology. Based on these new observations, an index will be established assembling the most discriminatory variables affecting populations at risk of consulting a doctor belatedly after the onset of the first cancer-related symptoms. Fundamentally, the data collected in the study will enable the testing and adjustment of health decision models. The understanding of the factors affecting health-related behavior will be improved, as will the methods used to prevent pathogenic behavior and promote protective behavior.

# 21 Strengths and limitations of the design

22 Because this design strives to understand the many determinants of delay and has important 23 implications for the literature as well as for implementing interventions, it is important to

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summarize its strengths and point out its limitations, inspired in part by the Aarhus checklist [42]. First, the beginning and the end points of the consultation delay are clearly defined and their assessment is therefore replicable. As the recall of the onset of symptoms may involve some recall biases, three measurements with different methods will be used to minimize the measurement error. Moreover, the self-assessment questionnaire including socio-cognitive and emotional determinants has been built to assess the specific hypotheses of this study. We have made this choice because 1) given the large range of variables studied, the use of specific validated questionnaires assessing each variable would be impossible, 2) some questionnaires (e.g. the importance of health in patients' personal priorities, their perceptions and reactions when they are faced with the onset of the first symptoms) do not exist, or have not yet been validated, or are difficult to find and 3) we have taken many precautions to build the scales on the basis of relevant and up-to-date theoretical models, inspired from previous studies, and the relevance and wording of items have been discussed carefully with several researchers involved in the care of head and neck cancer patients. We are convinced that all these methodological precautions will ensure the reliability of the data collected in this study.

# **Potential impacts**

During this study, the identification of new determinants explaining delayed consultation will enable a better targeting of the populations at risk of entering a treatment protocol at a late stage. The results of this study will improve the determination of individual and group factors that may explain patient delay in consulting for medical advice, an essential parameter in the prevention of abnormally high death rates and social inequality with regard to access to healthcare for patients with head and neck cancers. Knowledge of the socio-economic environment of the patient's living place, combined with individual socio-economic information, will enable the influence of the context on patient delay to be analyzed.

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However, it seems premature to design interventional studies straightaway, before the factors that are crucial and necessary for the formalization and setting up of such studies have been identified. The interests of specific health education systems, personalized screening, and healthcare interventions targeting populations at risk of delayed screening are undeniable. Depending on the results of this study, the populations considered at risk may, for example, be offered personalized psychosocial support, access to useful information to help them take health-related decisions, or easier access to the healthcare system and health-promoting systems. In addition, means may be implemented to increase the perceived capacity for action of at risk populations and their feelings of self-efficiency in terms of health.

The purpose of such operations would be to reduce diagnosis timelines in patients presenting with symptoms suggestive of head and neck cancers, with a view to (1) reducing the abnormally high death rates and changes in quality of life induced by delayed treatment and (2) fighting social inequality in terms of healthcare, a central component of the French Cancer Plan.

The authors declare that they have no competing interests.

#### **Author details**

VC, TL, MC, JF, and JLL contributed to the development and design of the protocol. CD and FV drafted the manuscript with critical input from all other authors who have read and approved the final manuscript.

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## **Figure legend**

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