



HAL
open science

Digestive cancer risk and occupational exposure in French farmers: results from Mutualité Sociale Agricole (MSA) medico-administrative databases

Baptiste Vesper Guillon

► To cite this version:

Baptiste Vesper Guillon. Digestive cancer risk and occupational exposure in French farmers: results from Mutualité Sociale Agricole (MSA) medico-administrative databases. Human health and pathology. 2019. dumas-02421826

HAL Id: dumas-02421826

<https://dumas.ccsd.cnrs.fr/dumas-02421826>

Submitted on 10 Jan 2020

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



AVERTISSEMENT

Ce document est le fruit d'un long travail approuvé par le jury de soutenance et mis à disposition de l'ensemble de la communauté universitaire élargie.

Il n'a pas été réévalué depuis la date de soutenance.

Il est soumis à la propriété intellectuelle de l'auteur. Ceci implique une obligation de citation et de référencement lors de l'utilisation de ce document.

D'autre part, toute contrefaçon, plagiat, reproduction illicite encourt une poursuite pénale.

Contact au SID de Grenoble :
bump-theses@univ-grenoble-alpes.fr

LIENS

Code de la Propriété Intellectuelle. articles L 122. 4
Code de la Propriété Intellectuelle. articles L 335.2- L 335.10

<http://www.cfcopies.com/juridique/droit-auteur>



UNIVERSITÉ GRENOBLE ALPES
UFR DE MÉDECINE DE GRENOBLE

Année : 2019

**DIGESTIVE CANCER RISK AND OCCUPATIONAL EXPOSURE IN FRENCH
FARMERS: RESULTS FROM MUTUALITE SOCIALE AGRICOLE (MSA)
MEDICO-ADMINISTRATIVE DATABASES**

THÈSE
PRÉSENTÉE POUR L'OBTENTION DU TITRE DE DOCTEUR EN MÉDECINE
DIPLOME D'ÉTAT

Baptiste VESPER GUILLON

[Données à caractère personnel]

THESE SOUTENUE PUBLIQUEMENT A LA FACULTE DE MEDECINE DE
GRENOBLE

Le Vendredi 27 Septembre 2019

DEVANT LE JURY COMPOSÉ DE

Président du jury :

M. le Professeur DECAENS Thomas

Membres :

M. le Professeur BONNETERRE Vincent

M. le Docteur SEIGNEURIN Arnaud

Mme le Docteur COSTENTIN Charlotte

Mme le Docteur HERVÉ Camille (directrice de thèse)

L'UFR de Médecine de Grenoble n'entend donner aucune approbation ni improbation aux opinions émises dans les thèses ; ces opinions sont considérées comme propres à leurs auteurs.

Doyen de la Faculté : Pr. Patrice MORAND

Année 2019-2020

ENSEIGNANTS DE L'UFR DE MEDECINE

CORPS	NOM-PRENOM	Discipline universitaire
PU-PH	ALBALADEJO Pierre	Anesthésiologie-réanimation et médecine péri-opératoire
PU-PH	APEL Florent	Ophthalmologie
PU-PH	ARVIEUX-BARTHELEMY Catherine	Chirurgie viscérale et digestive
PU-PH	BAILLET Athan	Rhumatologie
PU-PH	BARONE-ROCHETTE Gilles	Cardiologie
PU-PH	BAYAT Sam	Physiologie
MCF Ass.MG	BENDAMENE Farouk	Médecine Générale
PU-PH	BENHAMOU Pierre Yves	Endocrinologie, diabète et maladies métaboliques
PU-PH	BERGER François	Biologie cellulaire
MCU-PH	BIDART-COUTTON Marie	Biologie cellulaire
PU-PH	BLAISE Sophie	Chirurgie vasculaire ; médecine vasculaire
MCU-PH	BOISSET Sandrine	Bactériologie-virologie
PU-PH	BOLLA Michel	Cancérologie-Radiothérapie
PU-PH	BONAZ Bruno	Gastroentérologie, hépatologie, addictologie
PU-PH	BONNETERRE Vincent	Médecine et santé au travail
PU-PH	BOREL Anne-Laure	Nutrition
PU-PH	BOSSON Jean-Luc	Biostatistiques, informatique médicale et technologies de communication
MCU-PH	BOTTARI Serge	Biologie cellulaire
PR Ass.MG	BOUCHAUD Jacques	Médecine Générale
PU-PH	BOUGEROL Thierry	Psychiatrie d'adultes
PU-PH	BOUILLET Laurence	Médecine interne
MCU-PH	BOUSSAT Bastien	Epidémiologie, économie de la santé et prévention
PU-PH	BOUZAT Pierre	Anesthésiologie-réanimation et médecine péri-opératoire
PU-PH	BRAMBILLA Christian	Pneumologie
PU-PH	BRAMBILLA Elisabeth	Anatomie et cytologie pathologiques
MCU-PH	BRENIER-PINCHART Marie Pierre	Parasitologie et mycologie
PU-PH	BRICAULT Ivan	Radiologie et imagerie médicale
PU-PH	BRICHON Pierre-Yves	Chirurgie thoracique et cardiovasculaire
MCU-PH	BRIOT Raphaël	Thérapeutique-médecine de la douleur
MCU-PH	BROUILLET Sophie	Biologie et médecine du développement et de la reproduction
PU-PH	CAHN Jean-Yves	Hématologie
PU-PH	CARPENTIER Patrick	Chirurgie vasculaire, médecine vasculaire
PR Ass.MG	CARRILLO Yannick	Médecine Générale
PU-PH	CESBRON Jean-Yves	Immunologie
PU-PH	CHABARDES Stephan	Neurochirurgie
PU-PH	CHABRE Olivier	Endocrinologie, diabète et maladies métaboliques
PU-PH	CHAFFANJON Philippe	Anatomie

CORPS	NOM-PRENOM	Discipline universitaire
PU-PH	CHARLES Julie	Dermato-vénérologie
MCF Ass.MG	CHAUVET Marion	Médecine Générale
PU-PH	CHAVANON Olivier	Chirurgie thoracique et cardio- vasculaire
PU-PH	CHIQUET Christophe	Ophthalmologie
PU-PH	CHIRICA Mircea	Chirurgie viscérale et digestive
PU-PH	CINQUIN Philippe	Biostatistiques, informatique médicale et technologies de communication
MCU-PH	CLAVARINO Giovanna	Immunologie
PU-PH	COHEN Olivier	Histologie, embryologie et cytogénétique
PU-PH	COURVOISIER Aurélien	Chirurgie infantile
PU-PH	COUTTON Charles	Génétique
PU-PH	COUTURIER Pascal	Gériatrie et biologie du vieillissement
PU-PH	CRACOWSKI Jean-Luc	Pharmacologie fondamentale, pharmacologie clinique
PU-PH	CURE Hervé	Cancérologie
PU-PH	DEBATY Guillaume	Médecine d'Urgence
PU-PH	DEBILLON Thierry	Pédiatrie
PU-PH	DECAENS Thomas	Gastro-entérologie, Hépatologie
PU-PH	DEMATTEIS Maurice	Addictologie
PU-PH	DEMONGEOT Jacques	Biostatistiques, informatique médicale et technologies de communication
MCU-PH	DERANSART Colin	Physiologie
PU-PH	DESCOTES Jean-Luc	Urologie
PU-PH	DETANTE Olivier	Neurologie
MCU-PH	DIETERICH Klaus	Génétique
MCU-PH	DOUTRELEAU Stéphane	Physiologie
MCU-PH	DUMESTRE-PERARD Chantal	Immunologie
PU-PH	EPAULARD Olivier	Maladies infectieuses ; Maladies tropicales
PU-PH	ESTEVE François	Biophysique et médecine nucléaire
MCU-PH	EYSSERIC Hélène	Médecine légale et droit de la santé
PU-PH	FAUCHERON Jean-Luc	Chirurgie viscérale et digestive
MCU-PH	FAURE Julien	Biochimie et biologie moléculaire
PU-PH	FERRETTI Gilbert	Radiologie et imagerie médicale
PU-PH	FEUERSTEIN Claude	Physiologie
PU-PH	FONTAINE Éric	Nutrition
PU-PH	FRANCOIS Patrice	Epidémiologie, économie de la santé et prévention
MCU-MG	GABOREAU Yoann	Médecine Générale
PU-PH	GARBAN Frédéric	Hématologie ; Transfusion
PU-PH	GAUDIN Philippe	Rhumatologie
PU-PH	GAVAZZI Gaétan	Gériatrie et biologie du vieillissement
PU-PH	GAY Emmanuel	Neurochirurgie
MCU-PH	GILLOIS Pierre	Biostatistiques, informatique médicale et technologies de communication
PU-PH	GIOT Jean-Philippe	Chirurgie plastique, reconstructrice et esthétique
MCU-PH	GRAND Sylvie	Radiologie et imagerie médicale
PU-PH	GRIFFET Jacques	Chirurgie infantile
MCU-PH	GUZUN Rita	Nutrition
PU-PH	HAINAUT Pierre	Biochimie et biologie moléculaire
PU-PH	HALIMI Serge	Nutrition
PU-PH	HENNEBICQ Sylviane	Biologie et médecine du développement et de la reproduction
PU-PH	HOFFMANN Pascale	Gynécologie-obstétrique

CORPS	NOM-PRENOM	Discipline universitaire
PU-PH	HOMMEL Marc	Neurologie
PU-MG	IMBERT Patrick	Médecine Générale
PU-PH	JOUK Pierre-Simon	Génétique
PU-PH	KAHANE Philippe	Physiologie
MCU-PH	KASTLER Adrian	Radiologie et imagerie médicale
PU-PH	KRAINIK Alexandre	Radiologie et imagerie médicale
PU-PH	LABARERE José	Epidémiologie, économie de la santé et prévention
MCU-PH	LABLANCHE Sandrine	Endocrinologie, diabète et maladies métaboliques
MCU-PH	LANDELLE Caroline	Bactériologie – virologie ; Hygiène hospitalière
PU-PH	LANTUEJOUL Sylvie	Anatomie et cytologie pathologiques
MCU-PH	LARDY Bernard	Biochimie et biologie moléculaire
MCU - PH	LE GOUELLEC Audrey	Biochimie et biologie moléculaire
PU-PH	LECCIA Marie-Thérèse	Dermato-vénérologie
MCF Ass.MG	LEDOUX Jean-Nicolas	Médecine Générale
PU-PH	LEROY Vincent	Gastroentérologie ; hépatologie ; addictologie
PU-PH	LETOUBLON Christian	Chirurgie viscérale et digestive
PU-PH	LEVY Patrick	Physiologie
PU-PH	LONG Jean-Alexandre	Urologie
MCU-PH	LUPO Julien	Bactériologie-virologie
PU-PH	MAGNE Jean-Luc	Chirurgie vasculaire ; Médecine vasculaire
MCU-PH	MAIGNAN Maxime	Médecine d'urgence
PU-PH	MAITRE Anne	Médecine et santé au travail
MCU-PH	MALLARET Marie-Reine	Hygiène hospitalière
PU-PH	MALLION Jean-Michel	Cardiologie
MCU-PH	MARLU Raphaël	Hématologie ; Transfusion
MCU-PH	MAUBON Danièle	Parasitologie et mycologie
PU-PH	MAURIN Max	Bactériologie-virologie
MCU-PH	MC LEER Anne	Histologie, embryologie et cytogénétique
MCU-PH	MONDET Julie	Histologie, embryologie et cytogénétique
PU-PH	MORAND Patrice	Bactériologie-virologie
PU-PH	MOREAU-GAUDRY Alexandre	Biostatistiques, informatique médicale et technologies de communication
PU-PH	MORO Elena	Neurologie
PU-PH	MORO-SIBILOT Denis	Pneumologie
MCU-PH	MORTAMET Guillaume	Pédiatrie
PU-PH	MOUSSEAU Mireille	Cancérologie
PU-PH	MOUTET François	Chirurgie plastique, reconstructrice et esthétique ; brûlologie
MCF Ass.MG	ODDOU Christel	Médecine Générale
MCU-PH	PACLET Marie-Hélène	Biochimie et biologie moléculaire
PU-PH	PAILHE Régis	Chirurgie orthopédique et traumatologie
PU-PH	PALOMBI Olivier	Anatomie
PU-PH	PARK Sophie	Hématologie ; Transfusion
PU-PH	PASSAGGIA Jean-Guy	Anatomie
PR Ass.MG	PAUMIER-DESBRIERES Françoise	Médecine Générale
PU-PH	PAYEN DE LA GARANDERIE Jean-François	Anesthésiologie-réanimation et médecine péri-opératoire
MCU-PH	PAYSANT François	Médecine légale et droit de la santé
MCU-PH	PELLETIER Laurent	Biologie cellulaire
PU-PH	PELLOUX Hervé	Parasitologie et mycologie

CORPS	NOM-PRENOM	Discipline universitaire
PU-PH	PEPIN Jean-Louis	Physiologie
PU-PH	PERENNOU Dominique	Médecine physique et de réadaptation
PU-PH	PERNOD Gilles	Médecine vasculaire
PU-PH	PIOLAT Christian	Chirurgie infantile
PU-PH	PISON Christophe	Pneumologie
PU-PH	PLANTAZ Dominique	Pédiatrie
PU-PH	POIGNARD Pascal	Bactériologie-virologie
PU-PH	POLACK Benoît	Hématologie
PU-PH	POLOSAN Mircea	Psychiatrie d'adultes
PU-PH	RAMBEAUD Jean-Jacques	Urologie
PU-PH	RAY Pierre	Biologie et médecine du développement et de la reproduction
MCU-PH	RENDU John	Biochimie et biologie moléculaire
MCU-PH	RIALLE Vincent	Biostatistiques, informatique médicale et technologies de communication
PU-PH	RIETHMULLER Didier	Gynécologie-obstétrique ; gynécologie médicale
PU-PH	RIGHINI Christian	Oto-rhino-laryngologie
PU-PH	ROMANET Jean Paul	Ophthalmologie
PU-PH	ROSTAING Lionel	Néphrologie
MCU-PH	ROUSTIT Matthieu	Pharmacologie fondamentale ; pharmacologie clinique ; addictologie
MCU-PH	ROUX-BUISSON Nathalie	Biochimie et biologie moléculaire
MCF Ass.MG	ROYER DE VERICOURT Guillaume	Médecine Générale
MCU-PH	RUBIO Amandine	Pédiatrie
PU-PH	SARAGAGLIA Dominique	Chirurgie orthopédique et traumatologie
MCU-PH	SATRE Véronique	Génétique
PU-PH	SAUDOU Frédéric	Biologie cellulaire
PU-PH	SCHMERBER Sébastien	Oto-rhino-laryngologie
PU-PH	SCHWEBEL Carole	Médecine intensive-réanimation
PU-PH	SCOLAN Virginie	Médecine légale et droit de la santé
MCU-PH	SEIGNEURIN Arnaud	Epidémiologie, économie de la santé et prévention
PU-PH	STAHL Jean-Paul	Maladies infectieuses ; Maladies tropicales
PU-PH	STANKE Françoise	Pharmacologie fondamentale
MCU-PH	STASIA Marie-José	Biochimie et biologie moléculaire
PU-PH	STURM Nathalie	Anatomie et cytologie pathologiques
PU-PH	TAMISIER Renaud	Physiologie
PU-PH	TERZI Nicolas	Médecine intensive-réanimation
MCU-PH	TOFFART Anne-Claire	Pneumologie
PU-PH	TONETTI Jérôme	Chirurgie orthopédique et traumatologie
PU-PH	TOUSSAINT Bertrand	Biochimie et biologie moléculaire
PU-PH	VANZETTO Gérard	Cardiologie
PU-PH	VUILLEZ Jean-Philippe	Biophysique et médecine nucléaire
PU-PH	WEIL Georges	Epidémiologie, économie de la santé et prévention
PU-PH	ZAOUTI Philippe	Néphrologie
PU-PH	ZARSKI Jean-Pierre	Gastroentérologie ; hépatologie ; addictologie

PU-PH : Professeur des Universités - Praticiens Hospitaliers
MCU-PH : Maître de Conférences des Universités - Praticiens Hospitaliers
PU-MG : Professeur des Universités de Médecine Générale
MCU-MG : Maître de Conférences des Universités de Médecine Générale
PR Ass.MG : Professeur des Universités Associé de Médecine Générale
MCF Ass.MG : Maître de Conférences Associé de Médecine Générale

REMERCIEMENTS

Au Professeur Thomas DECAENS, merci d'avoir accepté de présider cette thèse et de m'avoir fait l'honneur de ta grande disponibilité, de ton regard avisé et de ton soutien tout au long de ce travail. Merci également de ta présence, de ta bonne humeur et de ta sympathie tout au long de mon internat.

Au Professeur Vincent BONNETERRE, merci d'avoir partagé le fruit de vos travaux antérieurs et permis à ce projet d'aboutir. Je vous remercie sincèrement pour votre investissement, votre réactivité et l'aide précieuse que vous avez apportée à l'élaboration de cette thèse.

Au Docteur Arnaud SEIGNEURIN, merci beaucoup d'avoir accepté de juger ce travail et de l'enrichir grâce à vos remarques.

Au Docteur Charlotte COSTENTIN, merci de votre disponibilité et votre réactivité pour juger ce travail.

Au Docteur Camille HERVÉ, qui a accepté de se lancer dans la direction de cette thèse. Merci infiniment de m'avoir fait confiance. Si c'était à refaire, c'est avec toi que je voudrai recommencer.

À Charlotte Maugard, dont la contribution à cette étude est inestimable. Merci pour tout ce que tu as fait, le travail que tu as accompli est remarquable.

À Pierre-Emmanuel Colle pour ta relecture attentive et ton aide à rédiger cet article en anglais.

À tous les médecins du CHU, envers qui ma reconnaissance est immense pour avoir partagé leur passion du travail et m'avoir appris ce beau métier.

Au Docteur Pierre-Yves Eyraud, merci pour tous les enseignements dont vous m'avez fait profiter, pour votre écoute, votre patience et votre pédagogie. Merci également de m'accorder

votre confiance pour les deux prochaines années, je m'efforcerai chaque jour d'être à la hauteur de la mission que vous me confiez.

Au Docteur Aurélie Durand, tu as su à ta manière très personnelle, me pousser au-delà de mes limites pour en revenir meilleur, merci.

Au Docteur Nicolas Mathieu, pour la richesse de ta personnalité et la qualité de ton enseignement.

À tous ceux qui m'ont permis de devenir ce jeune docteur aujourd'hui, au Professeur Bonaz, Professeur Leroy, Professeur Zarski, Docteur Tuvignon, Victoire Granger, Marie-Noëlle Hilleret, Audrey Picot, Virginie Lloyd.

À l'équipe du CH de Chambéry qui m'a vu faire mes premiers pas d'interne : Maria qui m'a transmis sa passion de l'endoscopie, Olivier, Christophe, Simona, François, Hélène, Corinne.

À l'équipe médicale d'Annecy, pour ce semestre parfait et le calendrier dédié : Joanna, Frédéric, Emmanuel, Mathieu, Elsa, Isabelle, Aude et le grand Monsieur Capony. J'espère que nos routes se croiseront encore.

Aux services d'oncologie du CH d'Annecy et de radiothérapie du CH de Chambéry : merci de m'avoir accueilli et fait partager vos belles spécialités, loin de la gastro-entérologie.

À mes co-internes passés et actuels :

À Laurine, merci d'avoir illuminé mon internat par ta présence et ton soutien sans faille. Je suis heureux de t'avoir à mes côtés.

À Mélodie, merci pour ces éclats de rire, la sincérité de nos discussions et la richesse de nos échanges.

À Justine, merci pour ta bonne humeur constante, ta sympathie à toute épreuve, ton intelligence. Le médecin parfait c'est toi.

À Aude, merci pour ton humour décapant et ta spontanéité. Tu pars pour plusieurs mois d'aventure et j'ai déjà hâte de te revoir.

À Bleuenn, Laurence, Loïc le presque pas stressé, Thomas mon mentor, Gaël mon plus grand professeur, Théo l'ami des soirées infirmières, Sandie, Olivier, Dysmas, Marion.

Aux plus jeunes que j'espère encore croiser avec plaisir, Sabine, Marion (Arc'teryx forever), Sylvain, Alia, Fabien, Pauline, Laetitia, Sophie, Juliette, Olivier, Thomas, Victoria.

Aux infirmiers et aides-soignants que j'ai eu la chance de rencontrer :

À Marine, mon petit chat, ta gentillesse, ta sincérité et ta dévotion sont des qualités précieuses, je suis heureux de t'avoir à mes côtés.

À Margaux, l'amie rêvée, garde ton sourire pétillant et ta bonne humeur.

À Emilie, merci pour ces belles discussions à des heures tardives.

À Seb et Yves, les représentants de la parité dans l'équipe infirmière.

À Sylvie, merci pour ta gentillesse, ton écoute et ta générosité. Tu me rappelles chaque jour que notre travail, c'est pour les patients que nous le faisons et je t'en suis reconnaissant.

À Anne, qui n'a pas sa langue dans sa poche mais qu'on aime pour ça.

À Amélie, Stéphanie, Aurore, Méline, Sana, Cindy, Sandy, Lucile, Magali et tant d'autres, qui m'ont accompagné depuis mon début d'internat. C'était un plaisir d'être à vos côtés.

Aux infirmier(e)s d'endoscopie que je m'apprête à retrouver avec joie. À Arlette, la dame de fer, merci pour ton aide précieuse au quotidien.

Aux infirmières et aides-soignants d'Annecy, travailler avec vous c'était un vrai bonheur.

Aux secrétaires médicales qui travaillent souvent dans l'ombre mais sans qui on ne ferait rien.

À mes amis :

À ceux qui ont fait ces longues études avec moi depuis le tout début, Magali, Céline, Méja, Sandie, Bérangère, ou à ceux que j'ai rejoint plus tard, Flora et Thomas.

À Sandra, qui a toujours été là et qui me supporte depuis toutes ces années. Que de rebondissements depuis les soirées en P2 jusqu'aux ours du Montana. A chaque moment important de ma vie tu étais là... Je ne te remercierai jamais assez.

À Claire, mon amie depuis les bancs d'école primaire, presque ma sœur, presque mon âme-sœur. Quand on est ensemble il ne peut rien nous arriver.

À Caroline et Carole, loin des yeux mais près du cœur.

À William, qui me rappelle que pharmacien et médecin peuvent bien s'entendre.

À Xavier, mon partenaire dans la quête de liberté.

Enfin à ma famille qui, à sa façon me témoigne son amour au quotidien. Vous êtes les piliers de ma vie. Merci pour tout.

Au petit Joan, qui brille parmi nous.

SOMMAIRE

REMERCIEMENTS	6
RÉSUMÉ	10
ABSTRACT	12
ABRÉVIATIONS	14
ARTICLE	15
INTRODUCTION	15
METHODS	17
RESULTS	19
DISCUSSION	21
CONCLUSION	25
REFERENCES	33
CONCLUSION	36
SERMENT D’HIPPOCRATE	37

**ÉVALUATION DU RISQUE DE CANCERS DIGESTIFS SELON L'EXPOSITION
PROFESSIONNELLE CHEZ LES AGRICULTEURS FRANÇAIS, D'APRÈS LES
DONNÉES MÉDICO-ADMINISTRATIVES DE LA MUTUALITÉ SOCIALE
AGRICOLE (MSA)**

RÉSUMÉ

Introduction : Les travailleurs agricoles ont un plus faible risque de cancer digestif. Il s'agit pourtant d'une population fréquemment exposée à de nombreux risques professionnels, parmi lesquels figuraient certains agents classés cancérigènes certains par le CIRC, et figurent toujours certains agents classés cancérigènes probables ou possibles, avec des variabilités d'exposition au sein des différentes activités agricoles. Le but de cette étude était d'évaluer le risque de cancer digestif en fonction de l'exposition professionnelle chez les agriculteurs français.

Méthodes : L'ensemble des exploitants agricoles ayant cotisé au moins une fois à la MSA entre 2006 et 2016 a été étudié. Les déclarations de cancers digestifs en ALD 30, au sein de cette population, ont été relevées de 2012 à 2016, en précisant le sous-type de cancer selon la classification CIM-10. A l'aide de modèles logistiques, permettant l'ajustement sur le sexe, l'âge et d'autres variables, les associations entre déclaration de cancers digestifs et activités agricoles ont été étudiées et exprimées sous forme d'Odds Ratio. Une correction (Benjamini-Hochberg) a été effectuée pour prendre en compte les tests multiples.

Résultats : Sur les 899 212 exploitants agricoles étudiés, 4438 cancers digestifs ont été déclarés. Le risque de cancer digestif était augmenté chez les viticulteurs (OR=1.28 [95% CI 1.16-1.42], $p<0.00005$), principalement lié à une augmentation du risque de cancer colorectal (OR=1.21 [95% CI 1.09-1.35], $p=0.01$). Une tendance à l'augmentation du risque de cancer du grêle a également été mise en évidence (OR=2.19 [95% CI 1.31–3.67], proche de la significativité ($p=0.07$ après application de la correction concernant les tests multiples). Par ailleurs, une diminution du risque de cancer digestif a été retrouvée chez les producteurs céréaliers (OR=0.87 [95% CI 0.8–0.95]), sous-tendue par une diminution de risque de cancer de l'estomac (OR=0.6 [95% CI 0.45–0.81]).

Conclusion : Nos résultats montrent une augmentation de risque de déclaration en ALD de cancer digestif et principalement de cancer colorectal chez les viticulteurs français. Il est également retrouvé une diminution du risque de cancer digestif chez les producteurs céréaliers, principalement une diminution de risque de cancer de l'estomac.

MOTS CLÉS : Cancers digestifs ; Agriculteurs ; Exposition professionnelle ; Facteurs de risque ; Cohorte

FILIÈRE : Gastro-entérologie, hépatologie et oncologie digestive, CHU Grenoble Alpes, France

**DIGESTIVE CANCER RISK AND OCCUPATIONAL EXPOSURE IN FRENCH
FARMERS: RESULTS FROM MUTUALITE SOCIALE AGRICOLE (MSA)
MEDICO-ADMINISTRATIVE DATABASES**

ABSTRACT

Introduction - Farmers are at lower risk to present with digestive cancer. However, this population is frequently exposed to carcinogens, with exposure variability depending on the agricultural activity. The aim of our study was to evaluate the risk of digestive cancer according to agricultural activity among French farmers.

Methods - We included all farmers recorded at least once in the social security system of French agricultural workers “Mutualité sociale agricole” (MSA) between January 2006 and December 2016. We recorded the digestive cancers in this population reported as Long Term Disease (LTD) from January 2012 to December 2016. We specified for each case the cancer subtype according to the ICD-10 classification. The association between digestive cancer and agricultural activity was studied with logistic models, and expressed as Odds Ratio

Results - 4,438 digestive cancers were reported among 899,212 included farmers. The risk of presenting with digestive cancer was increased in wine growers (OR=1.28 [95% CI 1.16-1.42]), mainly an increased risk of colorectal cancer (OR=1.21 [95% CI 1.09-1.35]). An increased risk of small bowel cancer was also identified but with a limited statistical significance (OR=2.19 [95% CI 1.31-3.67], p=0.08). Furthermore, a lower risk of digestive

cancer was identified among cereal crop farmers (OR=0.87 [95% CI 0.8-0.95]), supported by a lower risk of stomach cancer (OR=0.6 [95% CI 0.45-0.81]).

Conclusion - Our results suggest an increased risk of digestive cancer among French wine growers, mainly colorectal cancer. We also found a lower risk of digestive cancer among cereal crop farmers, mainly gastric cancer.

KEYWORDS - Gastrointestinal Neoplasms; Farmers; Risk Factors; Occupational Exposure; Cohort Studies

ABRÉVIATIONS

AGRICAN: AGRiculture and CANcer cohort

AHS: Agricultural Health Study

CI: Confidence Interval

IARC: Agency for Research on Cancer

ICD-10: International Classification of WHO Diseases, 10th edition

LTD: Long Term Disease

MCE: Matrice Culture Exposition

MSA: Mutualité Sociale Agricole

OR: Odds Ratio

ARTICLE

DIGESTIVE CANCER RISK AND OCCUPATIONAL EXPOSURE IN FRENCH FARMERS: RESULTS FROM MUTUALITE SOCIALE AGRICOLE (MSA) MEDICO-ADMINISTRATIVE DATABASES

INTRODUCTION

Cancer epidemiology

France has one of the highest incidence of cancer among European countries: 382,000 new cases were reported in 2018 [1]. Globally, it is estimated that one in five men and one in six women will develop cancer during their lifetime [2]. In terms of mortality, 157,000 deaths were cancer related in France, in 2018, making it the leading cause of specific mortality, regardless of gender, before cardiovascular diseases and infectious causes, despite recent and ongoing progress in early detection and treatment [1].

Digestive cancers

The incidence of digestive cancers is high in France, with colorectal cancer ranking first. The aging population, improved screening techniques, but also changes in lifestyle such as increased level of inactivity, have probably led an increased incidence since the 1980s. In 2017, there were an estimated 45,000 new cases per year of colorectal cancer, making it the second most common cancer in women and the third most common in men [3]. It is also one of the deadliest since it is ranked third in men and second in women in terms of mortality [3][4]. A rapid and poorly explained increase in the incidence of pancreatic cancer has also been reported over the past ten years (+ 2.7% per year in men and + 3.8% in women between

1990 and 2018), while these figures have not increased similarly in other industrialized countries [3] [5] [6].

Risk factors and occupational exposures

A study by the International Agency for Research on Cancer (IARC) in 2000 shows that about 35% of incident cancers could be preventable if exposure to risk factors had been at the optimal level or reference level [7]. Numerous published IARC monographs list the various types of known or suspected carcinogens, whether chemical, physical, viruses, dust, ionizing radiation, but also new lifestyle factors such as food quality. Tobacco and alcohol are the best-known and incriminated risk factors, accounting respectively for 20% and 8% of incident cancers [8][9]. Food consumption and obesity both account for 5.4% of the fractions attributable to new cases. Regular physical activity could be a protective factor [10]. 3.6% of incident cancers are attributable to occupational exposure and 12% of employees have been exposed at their workplace to at least one carcinogen (chemical or non-chemical), for occupational medicine [7]. More specifically for digestive cancers, the attributable fractions to occupational exposure were respectively 4% for stomach, 2% for colon-rectum, and 3.7% for liver cancer [9]. Studies focusing on a relationship between occupational exposure and cancer risk are valuable tools for prevention campaigns and the legal framework of product use.

Agricultural workers

The relationship between cancer and agriculture has been studied often since the early 1980s and has led to several meta-analyses [11] [12]. The authors of previous major studies have reported a reduction of cancer risk in this population compared to the global population, concerning digestive cancers [13]. Two major agricultural cohorts have allowed confirming

this: the Agricultural Health Study (AHS) among US private pesticide applicators from North Carolina and Iowa [14][15] and the AGRICulture and CANcer (AGRICAN) cohort among French farmers [16]. Possible explanations were a lower rate of tobacco consumption in this population high levels of occupational physical activity, and possibly a safer diet (higher fruits and vegetables intake). In the AGRICAN cohort, however, there was a slightly increased risk of stomach cancer in female farmers and in those who never used pesticides.

However, farmers are frequently exposed to many potentially carcinogenic agents such as pesticides, cristalline silica, ultraviolet rays, and viruses.[17].

Monitoring diseases in this exposed population is crucial for the identification and prevention of the new threats. Using insurance data for the detection of these risks, complementary to conventional epidemiological studies, could improve early detection.

The Mutualité Sociale Agricole (MSA) is a social security system covering all French agricultural workers for the following issues : diseases, family, occupational health and retirement. The MSA has undertaken to use its medico-administrative data for research purposes mainly on occupational risks vigilance. We decided to use these medico-administrative databases in our study to identify, without any prior assumption, any association between various agricultural activities and the occurrence of digestive cancers.

METHODS

Agreements

The massive data mining project in which this study is integrated was approved by the French Data Protection Authority CNIL (MMS/SBM/AE171001).

Study Population

The authors of a pilot study demonstrated the feasibility and relevance of MSA medico-administrative database use to assess risks among agricultural workers [18]. We used this cohort by focusing specifically on digestive cancers. MSA is the French national health insurance for every agricultural worker. It groups two different statuses of agricultural workers: farm owners and farm salaried workers, whether active or retired. They can be farmers, breeders, but also less frequent occupations such as beekeepers, foresters, shellfish farmers, and even tertiary workers serving the agricultural population (bank, insurance and MSA workers themselves). In 2016, 3.3 million people were affiliated with the MSA. We included all adults 18 of age or more, men and women, active farm owners, recorded in the MSA at least once between 2006 and 2016 (Table 1). Farm workers (employees) were not included in the analysis as a large proportion of them have either seasonal jobs, or move shortly from one contract to another, which introduce a higher variability in their occupations, and makes the assessment of occupational activity more complex and less accurate, so less relevant for our analysis. We did not take into account farm owners retired before 2006 since we have no information about occupational activity for them.

Data collection

Data collected from the MSA records was divided in two different categories: administrative database and medico-administrative database. The administrative database was implemented in 2006 and included sex, date of birth, region of residence, socio-economic status, first year of activity and agricultural activity as defined by the MSA thesaurus (Table 2). Each individual had to report his agricultural activity once a year and was regularly controlled.

The medico-administrative database was implemented in 2012. We identified all Long-Term Disease (LTD) declarations and the corresponding disease sub-category following the International Classification of WHO Diseases (ICD-10) (Table 3) for every year in this

database. Chronic diseases such as cancers are reported to the health insurance system, in France, by family practitioners as LTDs so that patients can have free medical care adapted to the disease. LTD 30 is the code for malignant tumors. We collected all ICD-10 codes from C15 to C26 (digestive cancers) in the database, reported between January 2012 and December 2016. We decided to group some ICD-10 codes because of their clinical and epidemiological similarity, with the aim to increase statistical power. Malignant neoplasms of the colon were grouped with rectosigmoid junction and rectum neoplasms (C18, C19, and C20 respectively); gallbladder neoplasms were grouped with other and unspecified biliary tract neoplasms (C23 and C24 respectively).

Statistical analysis

Two matrices were generated with ICD-10 codes on one hand and occupational activities on the other hand, studied as binary variables. Each association between one ICD-10 code and one occupational activity was studied with a specific model build with stepwise selection of variables. Because of the great number of tests, it was essential to control the potentially false identifications and highlight the relevant associations. We chose the Benjamini-Hochberg procedure, stable but little conservative, to adjust p-values. We calculated p-values for each association, with an alpha risk of 0.05. P-values <0.05 , after correction for multiple testing, were considered as statistically significant. Results were computed as Odds Ratio (OR) expressed with a 95% confidence interval (CI), adjusted on age, sex, year of first installation, matrimonial status, affiliation status, region, exploitation administrative area, and history of any LTD. All statistical analyses were performed using R statistical software.

RESULTS

Study Population

The main characteristics of the study population are listed in Table 1. 899,212 farm-owners were identified; mostly men (70.2%) with a median age of 50.2 years (± 12.9 for men and ± 13.5 for women), median year of first installation in 1995 (1940 to 2016), and 69.5% were exclusively working in agriculture. We identified, for the five main activities, 226,607 (23%) people working in cereal crops, 136,146 (13.8%) in dairy cattle, 104,128 (10.6%) in winegrowing, 101,711 (10.3%) in beef cattle, and 112,983 (11.5%) in mixed crops and breeding.

Occupational exposure and cancer risk

We identified 4,438 digestive cancers (Table 4) between January 2012 and December 2016. Colorectal cancer was the most frequent subtype (n=2,930; 66%), followed by pancreatic cancer (n=434; 9.8%), gastric cancer (n=314; 7%), esophagus cancer (n=290; 6.5%), and liver and intrahepatic bile ducts cancer (n=260; 5.9%). The associations between occupational activities and occurrence of digestive cancer are listed in Table 5 and Table 6

Winegrowing

Winegrowing was associated with an overall increased risk of digestive cancer of nearly 30% (OR=1.28, 95%CI 1.16–1.42; $p < 0.00005$). The risk increase was preponderant for colorectal cancer, nearly 20%, resistant to correction of multiple tests (OR=1.21, 95%CI 1.09–1.35; $p = 0.01$). We found a higher risk of small intestine cancer for winegrowing before multiple test correction (OR=2.19, 95%CI 1.31–3.67), still nearly significant, after Benjamini-Hochberg correction ($p = 0.07$). The high level of statistical significance for all cancers OR estimate is partly due to the fact that, except for esophagus, all cancer risks estimates were above 1, even if none of them, except for colorectal cancer, was statistically significant by itself.

Cereal crop

We found an overall lower risk for all digestive cancers in cereal crop farmers, of nearly 13% (OR=0.87, 95%CI 0.8–0.95; p=0.02) and more specifically a significantly lower risk of 40% of stomach cancer (OR=0.6, 95%CI 0.45–0.81; p=0.02).

Negative but non-significant associations were identified for cereal crop farmers: esophagus cancer (OR=0.97, 95%CI 0.73–1.28), colorectal cancer (OR=0.95, 95%CI 0.87–1.04), liver and intrahepatic bile duct cancer (OR=0.9, 95%CI 0.67–1.23), and pancreatic cancer (OR=0.97, 95%CI 0.77–1.23).

Other occupational activities

No significant difference in risk was identified for other cancer sites such as esophagus, liver and bile ducts, pancreas, anal canal, regardless of occupational activity.

DISCUSSION

This large-scale study highlighted an increased risk of digestive cancer and more specifically of colorectal cancer among French winegrowers. It also highlighted a reduction in the risk of stomach cancer in cereal crop farmers.

Limitation and strength of our study

The first strength of this study was the great number of farmers of both genders included, and the diversity in activity. It was also the extensive data collection for farm-owners since the MSA is the only social regimen for these professionals in France.

The follow-up period was long, since the median year of installation was 1995 and the first recorded agricultural activity went back to 1940. Cancer declarations have been recorded since 2012, allowing for a delay between professional exposure and occurrence of cancer consistent with the current data on carcinogenic processes [19][20][21][22][23].

We performed a robustness test, to avoid the risk of over-adjustment, by limiting the number of adjustment variables. We kept only age, sex, year of installation, health regimen, and geographic region. The results obtained were the same as in the main analysis, reinforcing the power of our study.

Our study however, had several limitations. The occupational activity was assessed as an exposed / not exposed dichotomous form. Our data prevent us to take into account the duration of activity and thus the duration of exposure, whereas we suppose that the real risk depend on cumulative exposure, and that exposure might have change over successive periods (change in pesticides use, etc).

We were unable to include tobacco abuse status in the adjustment variables since this data was not present in the MSA records. However, it is well known that tobacco abuse among farmers is lower than in the global population (21% vs. 34% respectively), which would tend to support our results [24].

We chose to include only farm-owners because they were considered as more stable in their professional activity, whereas it was difficult to establish a work time threshold for farm-salaried-workers that could be qualified as "stable". In the Maugard pilot study, 75% of employees had to be excluded because they did not meet the criteria for stable employment

(>1,014h / year) [18]. The AGRICAN cohort, however, showed a slightly increased cancer risk in the farm-worker subgroup compared to farm-owners (+ 14%). Not taking this subpopulation into account was therefore a limitation of our study, but a database review is ongoing to include them in the near future.

Differences between observed and predicted incidence using the LTD variable were assessed in French administrative subdivision using a cancer registry [25]. This method was chosen to estimate the overall incidence of colorectal cancer in France from data in administrative subdivision with a cancer registry, with a relative error of prediction inferior to 15%. The authors showed that the use of French National Hospital Information System (PMSI, Programme de Médicalisation des Systèmes d'Information) data combined with LTD allowed improving the quality of incidence prediction for pancreatic, esophagus, and stomach cancer. It is therefore possible that incidence for these locations are higher than the occurrence found in our study, which could decrease the risk estimate for these cancers. Completing our study with hospital PMSI data could improve our results. Furthermore, the MSA medico-administrative database also contains data on medicine consumption. Integrating this data with the LTD declaration could help identify more patients with cancer.

Winegrowing

Published data concerning associations between winegrowing and digestive cancer risk is scarce. Some authors have shown an increased risk of rectosigmoid junction carcinoma among residents of a German winegrowing community (area under wine cultivation >20% of community area), but with no excess of cancer of either colon, rectum, or colon and sigmoid and rectum all together [26]. Thus, this result might be due to chance. This population was also characterized by an overall lower risk of digestive cancers. Winegrowing is the

agricultural activity in which pesticides are the most used in France (20% of pesticides for only 3% of the country's agricultural area). One of the main reasons for this increased risk could be the use of arsenic. Arsenical pesticides have been banned since 1973, except for winegrowing where they were allowed until 2001. It is estimated that between 1979 and 2001, from 60,000 to 100,000 winegrowers used this type of pesticide [27]. Inorganic arsenic is classified as carcinogenic to humans (group 1) by IARC and several authors have well documented the link between its use and the risk of skin, lung, bladder, prostate, and liver cancer [28][29][30]. A decreased incidence of colorectal cancer was reported after decreasing arsenic levels in drinking water but an increased risk of cancer was reported in individuals exposed to high levels of arsenic in drinking water [31][32]. Several animal and in vitro models support the potential carcinogenic role of arsenic in colorectal cancer [33][34]. In contrast, research has highlighted the therapeutic potential of arsenical derivatives in the treatment of digestive cancers [35][36].

Cereal crops

We observed a lower risk of digestive cancers and mainly gastric cancers in cereal crop growers. The AGRICAN cohort has already proved a lower risk of gastric cancer among male farm-owners. The link with occupational exposure is not established and it is likely that the environment, especially dietary patterns, play a role in this risk variability. Several protective associations for gastric cancer have already been demonstrated such as the consumption of fruits, vegetables, and dietary flavonoids [37][38]. In contrast, high salt intake or red and processed meat consumption may be associated with an increased risk of gastric cancer [39][40].

Research perspectives

The MSA administrative database includes the region of activity for each farmer. We could study the geographical distribution of cancer declaration rates and compare them with data published by the National Public Health Agency (*Santé Publique France*).

Moreover, winegrowing has a strong north-south distribution gradient in France. It would be interesting to know if this gradient could be identified in the occurrence of colorectal cancer in our study.

Finally, this exploratory preliminary study could be extended by identification of phytosanitary product use by farmers. The Graphical Terrain Register (Registre Parcellaire Graphique) lists all French agricultural areas and their main cultures. Furthermore, the Crop Exposure Matrices (MCE) of the Matphyto project of the National Public Health Agency (*Santé Publique France*) allows the evaluation of retrospective phytosanitary product exposure according to agricultural specialty [41]. We could evaluate the association between phytosanitary product use and digestive cancer by associating these tools with our study models [42]. We could thus improve vigilance for phytosanitary product use among farmers.

CONCLUSION

We found a positive association between winegrowing and the occurrence of LTD digestive cancers among French farm-owners, most often colorectal cancer. We question the use of arsenic as a pesticide until 2001 in this population to be one of the possible risk factors. We also highlighted a reduction in the risk of stomach cancer in cereal crop farmers.

The evaluation of occupational exposure is a major challenge to detect new risks and protect agricultural workers. Further studying the associations between phytosanitary product use and cancer risk could provide crucial answers to these topical issues.

Table 1

Main characteristics of study population made of French self-employed agricultural workers

Characteristics	N	%
Overall	899,212	-
Gender		
Men	631,560	70.2
Women	267,652	29.8
Mean age		
Men	48.7	-
Women	53.8	-
Year of first installation		
Median	1995	-
Minimum	1940	-
Maximum	2016	-
Health regimen		
Exclusive	625,139	69.5
Principal	42,077	4.7
Liberal	10,463	1.2
Employees	16,959	1.9
Others	204,574	22.8
Matrimonial status		
Single	350,942	39.0
Married	532,732	59.2
Widowed	37,940	4.2
Divorced	48,366	5.4

¹Health regimen: exclusive: 100% incomes from agriculture. Principal: > 50% incomes from agriculture. Liberal: < 50% incomes from agriculture. Others: simultaneous assignment to another health regimen

Table 2

Agricultural activities as defined by MSA thesaurus for self-employed workers

Value	Name
1	Vegetables, flowers
2	Fruit trees
3	Plant nursery
4	Cereals
5	Winegrowing
6	Forestry
7	Other specialized crops
8	Dairy cattle farmers
9	Beef farmers
10	Mixed dairy and beef cattle
11	Sheep and goat
12	Pigs
13	Horses
14	Other big animals
15	Poultry and rabbits
16	Other small animals
17	Horse riding club
18	Shellfish farming
19	Non-specialized and/or mixed crops and breeding
20	Salt marshes
21	Wood working
22	Sawmills
23	Agricultural company
24	Landscaping
25	Local agricultural health insurance agents

Table 3
ICD-10 classification for malignant digestive neoplasms

Code	Name
ICD-15	Malignant neoplasm of esophagus
ICD-16	Malignant neoplasm of stomach
ICD-17	Malignant neoplasm of small intestine
ICD-18	Malignant neoplasm of colon
ICD-19	Malignant neoplasm of rectosigmoid junction
ICD-20	Malignant neoplasm of rectum
ICD-21	Malignant neoplasm of anus and anal canal
ICD-22	Malignant neoplasm of liver and intrahepatic bile ducts
ICD-23	Malignant neoplasm of gallbladder
ICD-24	Malignant neoplasm of other and unspecified parts of biliary tract
ICD-25	Malignant neoplasm of pancreas
ICD-26	Malignant neoplasm of other and ill-defined digestive organs

Table 4 - Number of cancer cases following occupational exposures

	Vegetables, flowers	Fruit trees	Plant nursery	Cereal	Winegrowing	Forestry	Other specialized crops	Dairy cattle farmers	Beef farmers	Mixed dairy and beef	Sheep and goat	Pigs	Horses	Other big animals	Poultry and rabbits	Other small animals	Horse riding club	Shellfish	mixed crops and breeding	Salt marshes	Wood working	Sawmill	Agricultural company	Landscaping	Insurance agents	Rural artisans	
	185	125	16	1211	644	12	26	661	596	153	177	74	44	6	88	40	28	7	517	2	38	1	62	116	6	1	
ICD-15 esophagus	290	18	6	1	75	30	1	3	38	35	12	9	6	7	2	10	0	1	0	39	1	2	1	2	8	0	0
ICD-16 stomach	314	8	9	2	63	39	1	3	59	51	12	19	5	2	0	9	4	2	1	35	0	5	0	2	10	1	0
ICD-17 small intestine	83	3	3	0	18	19	0	0	13	15	3	1	0	2	0	1	1	1	0	6	0	0	0	0	2	1	0
ICD-18 colon	1935	71	54	7	560	275	4	10	293	240	58	76	34	16	2	32	18	12	3	220	0	12	0	30	45	2	0
ICD-19 rectosigmoid junction	220	9	7	0	61	42	0	3	28	30	8	4	3	4	0	3	3	1	0	20	0	3	0	5	6	0	0
ICD-20 rectum	824	43	19	2	221	117	6	3	114	119	25	26	15	3	0	21	7	3	1	95	0	7	0	11	18	1	1
ICD-21 Anus and anal canal	54	2	1	0	14	8	0	0	4	4	4	2	1	0	0	0	0	2	0	9	0	1	0	1	2	1	0
ICD-22 liver and intrahepatic bile ducts	260	9	7	1	66	36	0	0	35	31	13	11	3	3	0	6	1	2	2	32	1	6	0	5	6	0	0
ICD-23 gallbladder	24	1	0	0	9	4	0	0	3	6	0	1	0	2	0	0	0	0	0	1	0	0	0	0	1	0	0
ICD-24 other and unspecified parts of biliary tract	63	1	1	0	13	8	0	0	11	14	3	2	1	1	0	1	0	1	0	6	0	0	0	1	3	0	0
ICD-25 Pancreas	434	19	16	3	108	63	0	4	60	47	14	26	5	4	2	5	6	3	0	53	0	2	0	4	14	0	0
ICD-26 other and ill-defined digestive organs	20	1	2	0	3	3	0	0	3	4	1	0	1	0	0	0	0	0	0	1	0	0	0	1	1	0	0

Table 5 - Corrected p-values (Benjamini-Hochberg test) for associations between occupational exposures and digestive cancers

	ICD-15	ICD-16	ICD-17	ICD-18-19-20	ICD-21	ICD-22	ICD-23-24	ICD-25	ICD-26	ICD-15-26
Vegetables, flowers	2.52E-01	6.53E-01	0.998	0.791555556	0.998	0.998	0.998	0.984	0.999	0.788666667
Fruit trees	9.95E-01	9.64E-01	0.998	0.791555556	0.998	0.998	0.998	0.972	0.999	0.1235
Plant nursery	9.95E-01	9.64E-01		0.462222222		0.998		0.984		0.537333333
Cereal	9.95E-01	1.85E-02	0.998	0.496	0.998	0.998	0.998	0.984	0.999	0.02158
Winegrowing	9.31E-01	9.64E-01	0.07748	0.010972	0.998	0.998	0.998	0.972	0.999	0.0000455
Forestry	0.9308	0.964		0.182866667						0.432545455
Other specialized crops	0.51025	0.65288889		0.889473684		0.972				0.432545455
Dairy cattle farmers	5.10E-01	5.10E-01	0.998	0.481	0.7605	0.998	0.998	0.972	0.999	0.2496
Beef farmers	9.31E-01	5.10E-01	0.875333333	0.902	0.998	0.998	0.13754	0.972	0.999	0.869916667
Mixed dairy and beef	9.95E-01	9.64E-01	0.998	0.4732	0.7605	0.998	0.998	0.984	0.999	0.87
Sheep and goat	9.31E-01	5.10E-01	0.875333333	0.434571429	0.998	0.998	0.998	0.972		0.432545455
Pigs	9.31E-01	9.64E-01		0.434571429	0.998	0.998	0.998	0.984	0.999	0.2496
Horses	2.52E-01	9.53E-01	0.875333333	0.23595		0.998	0.5668	0.984		0.865913043
Other big animals	0.25168		0.434571429		0.972					0.537333333
Poultry and rabbits	2.52E-01	7.25E-01	0.998	0.902		0.998	0.998	0.972		0.437666667
Other small animals		9.64E-01	0.998	0.902		0.998		0.984		0.87
Horse riding club	9.31E-01	9.64E-01	0.998	0.7176	0.4251	0.998	0.998	0.984		0.537333333
Shellfish		0.964		0.599857143		0.998				0.432545455
Mixed crops and breeding	9.95E-01	9.64E-01	0.875333333	0.182866667	0.998	0.998	0.998	0.984	0.999	0.068986667
Salt marshes	0.25168		0.2977							0.6682
Wood working	0.995	0.65288889		0.902	0.998	0.2977		0.984		0.537333333
Sawmill	0.51025									0.537333333
Agricultural company	0.768444444	0.65288889		0.462222222	0.998	0.998	0.998	0.974	0.999	0.587052632
Landscaping	9.95E-01	9.64E-01	0.998	0.902	0.998	0.998	0.998	0.984	0.999	0.865913043
Insurance agents		0.5564	0.10647	0.791555556	0.11596					0.537333333
Rural artisans				0.481						0.432545455

Table 6 - Non-corrected p-values for associations between occupational exposures and digestive cancers

	ICD-15	ICD-16	ICD-17	ICD-18-19-20	ICD-21	ICD-22	ICD-23-24	ICD-25	ICD-26	ICD-15-26
Vegetables, flowers	4.84E-02	0.192	0.839	0.548	0.873	0.63	0.428	0.688	0.834	0.637
Fruit trees	6.66E-01	0.764	0.469	0.529	0.755	0.998	0.438	0.132	0.0479	0.019
Plant nursery	6.63E-01	0.855		0.16		0.726		0.667		0.372
Cereal	8.28E-01	0.00071	0.577	0.248	0.924	0.518	0.575	0.809	0.317	0.00166
Winegrowing	4.95E-01	0.822	0.00298	0.000422	0.628	0.429	0.699	0.17	0.751	0.00000175
Forestry	0.46	0.59		0.0211						0.152
Other specialized crops	0.13	0.226		0.65		0.257		0.154		
Dairy cattle farmers	1.57E-01	0.0785	0.721	0.209	0.0971	0.54	0.904	0.241	0.875	0.0492
Beef farmers	5.37E-01	0.0427	0.169	0.706	0.262	0.664	0.00529	0.267	0.318	0.803
Mixed dairy and beef	7.57E-01	0.713	0.89	0.182	0.117	0.158	0.951	0.709	0.786	0.87
Sheep and goat	4.16E-01	0.0761	0.202	0.117	0.829	0.91	0.735	0.0914		0.178
Pigs	3.98E-01	0.701		0.0843	0.767	0.823	0.88	0.56	0.248	0.0576
Horses	1.38E-02	0.403	0.158	0.0363		0.869	0.0436	0.801		0.766
Other big animals	0.048		0.109		0.299		0.372			
Poultry and rabbits	4.51E-02	0.279	0.531	0.779		0.463	0.579	0.125		0.202
Other small animals		0.687	0.766	0.856		0.304		0.459		0.837
Horse riding club	5.35E-01	0.768	0.563	0.414	0.0327	0.938	0.6	0.84		0.279
Shellfish		0.889		0.323		0.184		0.123		
Mixed crops and breeding	8.67E-01	0.447	0.121	0.0193	0.421	0.757	0.18	0.638	0.301	0.00796
Salt marshes	0.0249		0.0229		0.514					
Wood working	0.701	0.187		0.771	0.362	0.0155		0.464		0.343
Sawmill	0.146		0.346							
Agricultural company	0.266	0.217		0.155	0.652	0.777	0.931	0.337	0.178	0.429
Landscaping	9.59E-01	0.939	0.967	0.887	0.617	0.392	0.145	0.623	0.494	0.759
Insurance agents		0.107	0.00819	0.523	0.00446		0.335			
Rural artisans		0.222		0.183						

Table 7 - Odds Ratio for associations between occupational exposures and digestive cancers

	ICD-15	ICD-16	ICD-17	ICD-18-19-20	ICD-21	ICD-22	ICD-23-24	ICD-25	ICD-26	ICD-15-26
Vegetables, flowers	1.63 [1-2.64]	0.63 [0.31-1.27]	0.89 [0.28-2.81]	1.06 [0.88-1.28]	0.89 [0.22-3.66]	0.85 [0.43-1.67]	0.57 [0.14-2.31]	1.1 [0.69-1.75]	1.24 [0.17-9.29]	1.04 [0.87-1.24]
Fruit trees	0.83 [0.37-1.89]	1.11 [0.57-2.17]	1.53 [0.48-4.87]	1.08 [0.85-1.37]	0.73 [0.1-5.29]	1 [0.46-2.17]	0.46 [0.06-3.29]	1.48 [0.89-2.48]	4.42 [1.01-19.31]	1.28 [1.04-1.58]
Plant nursery	0.64 [0.09-4.66]	1.14 [0.28-4.65]		0.61 [0.31-1.21]		0.7 [0.09-5.19]		1.29 [0.4-4.11]		0.78 [0.45-1.35]
Cereal	0.97 [0.73-1.28]	0.6 [0.45-0.81]	0.86 [0.5-1.48]	0.95 [0.87-1.04]	1.03 [0.54-1.95]	0.9 [0.67-1.23]	0.86 [0.52-1.44]	0.97 [0.77-1.23]	0.52 [0.14-1.87]	0.87 [0.8-0.95]
Winegrowing	0.87 [0.6-1.28]	1.04 [0.74-1.46]	2.19 [1.31-3.67]	1.21 [1.09-1.35]	1.21 [0.57-2.57]	1.16 [0.81-1.66]	1.13 [0.61-2.08]	1.21 [0.92-1.59]	1.22 [0.36-4.2]	1.28 [1.16-1.42]
Forestry	2.1 [0.29-15.02]	1.72 [0.24-12.26]		2.09 [1.12-3.9]			1.62 [0.84-3.12]			
Other specialized crops	2.42 [0.77-7.57]	2.02 [0.65-6.33]		1.13 [0.67-1.9]			1.8 [0.65-5.01]		1.37 [0.89-2.11]	
Dairy cattle farmers	0.78 [0.55-1.1]	1.3 [0.97-1.73]	0.9 [0.49-1.63]	0.93 [0.84-1.04]	0.42 [0.15-1.17]	0.89 [0.62-1.29]	1.04 [0.58-1.85]	0.85 [0.64-1.12]	0.91 [0.26-3.15]	0.91 [0.82-1]
Beef farmers	0.89 [0.62-1.28]	1.37 [1.01-1.85]	1.48 [0.85-2.6]	1.02 [0.91-1.14]	0.56 [0.2-1.55]	0.92 [0.62-1.35]	2.05 [1.24-3.38]	0.84 [0.62-1.14]	1.75 [0.58-5.27]	1.01 [0.91-1.13]
Mixed dairy and beef	1.1 [0.61-1.97]	1.12 [0.62-1.99]	0.92 [0.29-2.93]	0.86 [0.69-1.07]	2.27 [0.81-6.34]	1.51 [0.85-2.66]	0.96 [0.3-3.06]	0.9 [0.53-1.55]	1.32 [0.18-9.98]	0.98 [0.82-1.19]
Sheep and goat	0.76 [0.39-1.48]	1.53 [0.96-2.44]	0.28 [0.04-1.99]	0.85 [0.69-1.04]	0.86 [0.21-3.52]	1.04 [0.56-1.92]	0.82 [0.26-2.6]	1.42 [0.95-2.13]		0.88 [0.73-1.06]
Pigs	1.42 [0.63-3.21]	1.19 [0.49-2.89]		1.29 [0.97-1.72]	1.35 [0.19-9.84]	0.88 [0.28-2.77]	0.86 [0.12-6.2]	0.77 [0.31-1.87]	3.32 [0.43-25.37]	1.29 [0.99-1.67]
Horses	2.64 [1.22-5.73]	0.55 [0.14-2.23]	2.77 [0.67-11.38]	0.62 [0.39-0.97]		1.1 [0.35-3.51]	3.32 [1.04-10.61]	0.88 [0.33-2.38]		0.95 [0.66-1.35]
Other big animals	4.24 [1.01-17.73]		0.29 [0.07-1.31]				2.16 [0.5-9.3]		0.6 [0.19-1.86]	
Poultry and rabbits	1.92 [1.01-3.63]	1.45 [0.74-2.82]	0.53 [0.07-3.84]	0.96 [0.73-1.26]		1.36 [0.6-3.08]	0.57 [0.08-4.13]	0.5 [0.2-1.21]		0.84 [0.65-1.1]
Other small animals		1.23 [0.45-3.33]	1.35 [0.19-9.84]	1.04 [0.7-1.53]		0.35 [0.05-2.57]		1.37 [0.6-3.13]		0.96 [0.66-1.4]
Horse riding club	0.54 [0.07-3.84]	0.81 [0.2-3.28]	1.79 [0.25-13.04]	0.81 [0.49-1.34]	4.78 [1.14-20.11]	1.06 [0.26-4.34]	1.7 [0.23-12.33]	0.89 [0.28-2.8]		0.77 [0.49-1.23]
Shellfish		1.15 [0.16-8.33]		0.6 [0.22-1.65]		2.71 [0.62-11.79]		0.41 [0.13-1.27]		
Mixed crops and breeding	1.03 [0.73-1.45]	0.87 [0.61-1.24]	0.52 [0.23-1.19]	0.87 [0.77-0.98]	1.34 [0.65-2.75]	0.94 [0.64-1.38]	0.59 [0.27-1.28]	0.93 [0.7-1.25]	0.35 [0.05-2.59]	0.86 [0.77-0.96]
Salt marshes	9.59 [1.33-69.17]					9.91 [1.37-71.53]		1.59 [0.4-6.41]		
Wood working	0.76 [0.19-3.08]	1.82 [0.75-4.44]		1.07 [0.69-1.64]	2.54 [0.34-18.81]	2.78 [1.21-6.35]		0.59 [0.15-2.4]		1.19 [0.83-1.71]
Sawmill	4.31 [0.6-30.88]						0.39 [0.05-2.77]			
Agricultural company	0.45 [0.11-1.83]	0.41 [0.1-1.68]		1.26 [0.92-1.73]	1.58 [0.22-11.55]	1.14 [0.45-2.88]	0.92 [0.13-6.64]	0.61 [0.22-1.68]	4.07 [0.53-31.34]	1.13 [0.83-1.54]
Landscaping	0.98 [0.47-2.03]	1.03 [0.53-1.97]	0.97 [0.23-4.06]	1.02 [0.79-1.31]	1.45 [0.34-6.31]	0.69 [0.3-1.61]	2.17 [0.77-6.17]	1.15 [0.66-2.01]	2.07 [0.26-16.6]	1.04 [0.83-1.29]
Insurance agents		5.06 [0.7-36.33]	14.75 [2.01-108.38]	1.45 [0.46-4.52]	18.37 [2.47-136.58]		1.62 [0.61-4.36]			
Rural artisans		0.29 [0.04-2.1]					0.26 [0.04-1.88]			

REFERENCES

- [1] Defossez G, Le Guyader-Peyrou S, Uhry Z, Grosclaude P, Colonna M, Dantony E, et al. Estimations nationales de l'incidence et de la mortalité par cancer en France métropolitaine entre 1990 et 2018. Synthèse. Saint-Maurice : Santé publique France, 2019. 20 p.
- [2] Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2018;68(6):394-424.
- [3] Jéhannin-Ligier K, Dantony E, Bossard N, Molinié F, Defossez G, Daubisse-Marliac L, Remontet L, Uhry Z. Projection de l'incidence et de la mortalité par cancer en France métropolitaine en 2017. Rapport technique. Saint-Maurice : Santé publique France, 2017. 80 p.
- [4] Santé publique France. Taux de participation au programme de dépistage organisé du cancer colorectal 2017-2018. 2019.
URL :<https://www.santepubliquefrance.fr/maladies-et-traumatismes/cancers/cancer-du-colon-rectum/articles/taux-de-participation-au-programme-de-depistage-organise-du-cancer-colorectal-2017-2018>
- [5] Ilic M, Ilic I. Epidemiology of pancreatic cancer. *World J Gastroenterol.* 28 nov 2016;22(44):9694-705.
- [6] Bouvier A-M, Uhry Z, Jooste V, Drouillard A, Remontet L, Launoy G, et al. Focus on an unusual rise in pancreatic cancer incidence in France. *Int J Epidemiol.* 01 2017;46(6):1764-72.
- [7] World Health Organization, International Agency for Research on Cancer (2007). Attributable Causes of Cancer in France in the Year 2000. IARC Working Group Reports, Vol. 3. Lyon, France: International Agency for Research on Cancer.
- [8] Marant Micallef C, Shield K, Vignat J, Hill C, Rogel A, Menvielle G, et al. Nombre et fractions de cancers attribuables au mode de vie et à l'environnement en France métropolitaine en 2015 : résultats principaux. *Bulletin Epidemiologique Hebdomadaire.* 26 juin 2018;
- [9] Marant Micallef C, Shield KD, Baldi I, Charbotel B, Fervers B, Gilg Soit Ilg A, et al. Occupational exposures and cancer: a review of agents and relative risk estimates. *Occup Environ Med.* août 2018;75(8):604-14.
- [10] Neugut AI, Terry MB, Hocking G, Mosca L, Garbowski GC, Forde KA, et al. Leisure and occupational physical activity and risk of colorectal adenomatous polyps. *Int J Cancer.* 11 déc 1996;68(6):744-8.
- [11] Acquavella J, Olsen G, Cole P, Ireland B, Kaneene J, Schuman S, et al. Cancer among farmers: a meta-analysis. *Ann Epidemiol.* janv 1998;8(1):64-74. PMID : 9465996.
- [12] Blair A, Zahm SH, Pearce NE, Heineman EF, Fraumeni JF. Clues to cancer etiology from studies of farmers. *Scand J Work Environ Health.* août 1992;18(4):209-15. PMID : 1411362.
- [13] Pukkala E, Martinsen JI, Lynge E, Gunnarsdottir HK, Sparén P, Tryggvadottir L, et al. Occupation and cancer - follow-up of 15 million people in five Nordic countries. *Acta Oncol.* 2009;48(5):646-790.
- [14] Alavanja MCR, Sandler DP, Lynch CF, Knott C, Lubin JH, Tarone R, et al. Cancer incidence in the agricultural health study. *Scand J Work Environ Health.* 2005;31 Suppl 1:39-45; discussion 5-7. PMID : 16190148.
- [15] Lerro CC, Koutros S, Andreotti G, Sandler DP, Lynch CF, Louis LM, et al. Cancer incidence in the Agricultural Health Study after 20 years of follow-up. *Cancer Causes Control.* avr 2019;30(4):311-22.
- [16] Lemarchand C, Tual S, Levêque-Morlais N, Perrier S, Belot A, Velten M, et al. Cancer incidence in the AGRICAN cohort study (2005-2011). *Cancer Epidemiol.* 2017;49:175-85.

- [17] Darcey E, Carey RN, Reid A, Driscoll T, Glass DC, Benke GP, et al. Prevalence of exposure to occupational carcinogens among farmers. *Rural Remote Health*. 2018;18(3):4348.
- [18] Maugard C, Rieutort DB, Ozenfant D, François O, Bonnetterre V. Big-data and occupational health surveillance: Screening of occupational determinants of health among French agricultural workers, through data mining of medico-administrative databases. *Revue d'Épidémiologie et de Santé Publique*. 1 juill 2018;66:S262-3.
- [19] Hisabe T, Hirai F, Matsui T. Development and progression of colorectal cancer based on follow-up analysis. *Dig Endosc*. avr 2014;26 Suppl 2:73-7.
- [20] Muto T, Bussey HJ, Morson BC. The evolution of cancer of the colon and rectum. *Cancer*. déc 1975;36(6):2251-70.
- [21] O'Connell B, Hafiz N, Crockett S. The Serrated Polyp Pathway: Is It Time to Alter Surveillance Guidelines? *Curr Gastroenterol Rep*. 29 août 2017;19(10):52.
- [22] Garnett MJ, Marais R. Guilty as charged: B-RAF is a human oncogene. *Cancer Cell*. oct 2004;6(4):313-9.
- [23] Brosens LAA, Hackeng WM, Offerhaus GJ, Hruban RH, Wood LD. Pancreatic adenocarcinoma pathology: changing « landscape ». *J Gastrointest Oncol*. août 2015;6(4):358-74.
- [24] Lauzeille D, Marchand J L, Ferrand M. Consommation de tabac par catégorie socioprofessionnelle et secteur d'activité – Outil méthodologique pour l'épidémiologie. Saint-Maurice (Fra) : Institut de veille sanitaire, juillet 2019, 208 p.
- [25] Chatignoux É, Remontet L, Colonna M, Grosclaude P, Decool E, Uhry Z. Estimations régionales et départementales d'incidence et de mortalité par cancers en France, 2007-2016. Évaluation de l'utilisation des données médico-administratives pour estimer l'incidence départementale : comparaison de l'incidence observée et prédite dans les registres sur la période 2007-2014. Saint-Maurice : Santé publique France, 2019. 106 p.
- [26] Seidler A, Hammer GP, Husmann G, König J, Krtshil A, Schmidtman I, et al. Cancer risk among residents of Rhineland-Palatinate winegrowing communities: a cancer-registry based ecological study. *J Occup Med Toxicol*. 6 juin 2008;3:12.
- [27] Spinosi J, Févotte J, Vial G. éléments techniques sur l'exposition professionnelle aux pesticides arsenicaux. Matrice cultures - expositions aux pesticides arsenicaux. Saint-Maurice (Fra) : Institut de veille sanitaire, avril 2009, 19 p.
- [28] International Agency on Research on Cancer, Arsenic and arsenic compounds, IARC Monographs on the Evaluation of Carcinogenic Risks to Humans Volume 100C, 2012.
- [29] Institut national de l'environnement industriel et des risques. Fiche toxicologique. Arsenic et composés minéraux. 2006, [11] 6 p.
- [30] Straif K, Benbrahim-Tallaa L, Baan R, Grosse Y, Secretan B, El Ghissassi F, et al. A review of human carcinogens--Part C: metals, arsenic, dusts, and fibres. *Lancet Oncol*. mai 2009;10(5):453-4.
- [31] Yang C-Y, Chang C-C, Ho S-C, Chiu H-F. Is colon cancer mortality related to arsenic exposure? *J Toxicol Environ Health Part A*. 2008;71(8):533-8.
- [32] Tsai SM, Wang TN, Ko YC. Mortality for certain diseases in areas with high levels of arsenic in drinking water. *Arch Environ Health*. juin 1999;54(3):186-93.
- [33] Cholpraipimolrat W, Suriyo T, Rangkadilok N, Nookabkaew S, Satayavivad J. Hijiki and sodium arsenite stimulate growth of human colorectal adenocarcinoma cells through ERK1/2 activation. *Food Chem Toxicol*. déc 2017;110:33-41.
- [34] Eyvani H, Moghaddaskho F, Kabuli M, Zekri A, Momeny M, Tavakkoly-Bazzaz J, et al. Arsenic trioxide induces cell cycle arrest and alters DNA methylation patterns of cell cycle regulatory genes in colorectal cancer cells. *Life Sci*. 15 déc 2016;167:67-77.

- [35] Ma Z-B, Xu H-Y, Jiang M, Yang Y-L, Liu L-X, Li Y-H. Arsenic trioxide induces apoptosis of human gastrointestinal cancer cells. *World J Gastroenterol*. 14 mai 2014;20(18):5505-10.
- [36] Lv X-H, Wang C-H, Xie Y. Arsenic trioxide combined with transarterial chemoembolization for primary liver cancer: A meta-analysis. *J Gastroenterol Hepatol*. sept 2017;32(9):1540-7.
- [37] Woo HD, Lee J, Choi IJ, Kim CG, Lee JY, Kwon O, et al. Dietary flavonoids and gastric cancer risk in a Korean population. *Nutrients*. 10 nov 2014;6(11):4961-73
- [38] Gonzalez CA, Lujan-Barroso L, Bueno-de-Mesquita HB, Jenab M, Duell EJ, Agudo A, et al. Fruit and vegetable intake and the risk of gastric adenocarcinoma: a reanalysis of the European Prospective Investigation into Cancer and Nutrition (EPIC-EURGAST) study after a longer follow-up. *Int J Cancer*. 15 déc 2012;131(12):2910-9.
- [39] Abnet CC, Corley DA, Freedman ND, Kamangar F. Diet and upper gastrointestinal malignancies. *Gastroenterology*. mai 2015;148(6):1234-1243.e4.
- [40] González CA, Jakszyn P, Pera G, Agudo A, Bingham S, Palli D, et al. Meat intake and risk of stomach and esophageal adenocarcinoma within the European Prospective Investigation Into Cancer and Nutrition (EPIC). *J Natl Cancer Inst*. 1 mars 2006;98(5):345-54.
- [41] Spinosi J, Févotte J. Le programme Matphyto—Matrices cultures-expositions aux produits phytosanitaires. Saint-Maurice (Fra): Institut de veille sanitaire, juin 2008, 16 p.
- [42] Achard P, Maugard C, Cancé C, Spinosi J, Ozenfant D, Maître A, et al. Medico-administrative data combined with agricultural practices data to retrospectively estimate pesticide use by agricultural workers. *J Expo Sci Environ Epidemiol*. 4 sept 2019.

THÈSE SOUTENUE PAR : Baptiste VESPER GUILLON

TITRE :

Evaluation du risque de cancers digestifs selon l'exposition professionnelle chez les agriculteurs français, d'après les données médico-administratives de la Mutualité Sociale Agricole (MSA)

CONCLUSION :

Les travailleurs agricoles ont un plus faible risque de cancer digestif. Il s'agit pourtant d'une population fréquemment exposée à des agents cancérigènes, avec des variabilités d'exposition au sein des différentes activités agricoles. Le but de cette étude était d'évaluer le risque de cancer digestif en fonction de l'exposition professionnelle chez les agriculteurs français.

L'ensemble des exploitants agricoles ayant cotisé au moins une fois à la MSA entre 2006 et 2016 a été étudié. Les déclarations de cancers digestifs en ALD 30, au sein de cette population, ont été relevées de 2012 à 2016, en précisant le sous-type de cancer selon la classification CIM-10. A l'aide de modèles logistiques, les associations entre déclaration de cancers digestifs et activités agricoles ont été étudiées et exprimées sous forme d'Odds Ratio.

Sur les 899 212 exploitants agricoles étudiés, 4438 cancers digestifs ont été déclarés. Le risque de cancer digestif était augmenté chez les viticulteurs (OR = 1.28 [95% CI 1.16-1.42]), principalement lié à une augmentation du risque de cancer colorectal (OR = 1.21 [95% CI 1.09-1.35]). Une augmentation du risque de cancer du grêle a également été mise en évidence mais de significativité statistique limite (OR = 2.19 [95% CI 1.31-3.67]). Par ailleurs, une diminution du risque de cancer digestif a été retrouvée chez les producteurs céréaliers (OR = 0.87 [95% CI 0.8-0.95]), sous-tendue par une diminution de risque de cancer de l'estomac (OR = 0.6 [95% CI 0.45-0.81]).

Nos résultats montrent une augmentation de risque de déclaration de cancer digestif et principalement de cancer colorectal chez les viticulteurs français.

VU ET PERMIS D'IMPRIMER

Grenoble, le :

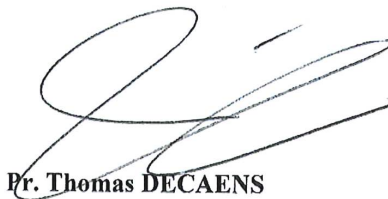
3/9/19

LE DOYEN

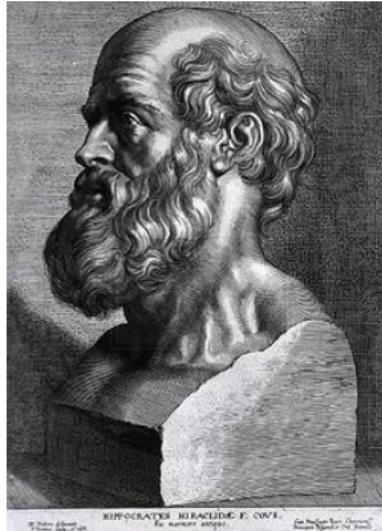


Pr. Patrice MORAND
Pour le Président
et par délégation
Le Doyen de Médecine
Pr. Patrice MORAND

LE PRÉSIDENT DE LA THÈSE



Pr. Thomas DECAENS



SERMENT D'HIPPOCRATE

En présence des Maîtres de cette Faculté, de mes chers condisciples et devant l'effigie d'HIPPOCRATE,

Je promets et je jure d'être fidèle aux lois de l'honneur et de la probité dans l'exercice de la Médecine.

Je donnerai mes soins gratuitement à l'indigent et n'exigerai jamais un salaire au dessus de mon travail. Je ne participerai à aucun partage clandestin d'honoraires.

Admis dans l'intimité des maisons, mes yeux n'y verront pas ce qui s'y passe ; ma langue taira les secrets qui me seront confiés et mon état ne servira pas à corrompre les mœurs, ni à favoriser le crime.

Je ne permettrai pas que des considérations de religion, de nation, de race, de parti ou de classe sociale viennent s'interposer entre mon devoir et mon patient.

Je garderai le respect absolu de la vie humaine.

Même sous la menace, je n'admettrai pas de faire usage de mes connaissances médicales contre les lois de l'humanité.

Respectueux et reconnaissant envers mes Maîtres, je rendrai à leurs enfants l'instruction que j'ai reçue de leurs pères.

Que les hommes m'accordent leur estime si je suis fidèle à mes promesses.

Que je sois couvert d'opprobre et méprisé de mes confrères si j'y manque.