RATIONALE: Globally, the mortality rate of people who inject drugs (PWID) is nearly 15 times greater than the general population [1]. Canadian evidence is scarce, however, and limited to the Vancouver context [1, 2]. Between 1996-2011, age-standardized mortality ratios of 7 and 16 were estimated for male and female PWID in Vancouver, with leading causes of death related to HIV/AIDS and overdose [2].

A comprehensive understanding of mortality rates and associated causes is essential to developing appropriate policies and interventions to reduce premature mortality in PWID. Yet in Québec, we lack the data necessary to guide these decisions. Temporal trends in mortality and associated causes remain poorly characterized in any part of the country, despite several major contextual shifts in the past two decades. These include the introduction and scale-up of efficient HIV therapies and associated declines in mortality [3, 4] and incidence among PWID [5], contrasted with a consistently high incidence of HCV infection [6-8]. We have also seen the gradual scale-up of preventive interventions including needle syringe programs, opiate agonist treatment, and recently, supervised consumption sites [9, 10], likely contributing to improved health outcomes.

While HIV and HCV infection are primary foci within our network, the opioid crisis sweeping across the country has rapidly become a public health emergency [6]. Cocaine has historically been the primary drug of injection in Canada [8], but the past decade has seen vast increases in opioid use, injection, and overdose-related deaths, claiming nearly 4500 lives in 2018 [11]. Though critical to inform public health priorities, the impact of these changes in drugs epidemics on drug-related deaths, relative to other causes, remains unknown in Québec.

The syndemic of overdose, infectious disease transmission, and other harms among PWID has flagged the deleterious role played by punitive drug policies [12-16]. Incarceration and the period post-release increase the risk of overdose and morality [17], HIV and HCV infection [18]. Despite profound variation in incarceration patterns and drug policies across countries [19, 20], little evidence on the relationship between incarceration and mortality among PWID exists in Canada. Recent data from our group [21] suggests that even short periods of detention (<1 week) and local jail stays, which are frequent in Québec [22, 23] and other provinces [24], may carry significant harm [21]. As decriminalisation of drug possession is becoming a focal political issue [25, 26], a closer examination of the relationship between detention patterns and mortality among PWID in a Canadian setting is particularly timely.

Since 1992, the St Luc/HEPCO cohort has followed >4000 PWID in Montréal. This study, one of eight cohorts in the Réseau SIDA-MI, has generated key insights into patterns of drug use and risk behaviours, [27-30] service use, [31, 32] and HIV/HCV [5, 33-37] among PWID. Yet it has not been exploited to study trends and determinants of mortality. By linking mortality records to the extensive cohort data, this proposal will launch new avenues for research and collaboration within the network and abroad. It will support new partnerships with young researchers specialised in the fields of mortality and prisoner health, expanding the breadth of the preventive research agenda for PWID and adding new horizons to this longstanding community-based research asset.

HYPOTHESES: Consistent with prior findings from other large urban settings in North America [1, 2], we expect age- and sex-standardized mortality rates to be higher among PWID relative to the general population of Québec. Meanwhile, the dominant causes of mortality among PWID are likely to have shifted significantly over time, with declining HIV/AIDS-related mortality and rising mortality due to HCV-related liver disease and overdose. We expect to see persistently greater excess mortality among women (relative to men) who inject drugs [1, 2], due to their marginalisation within PWID communities and poorer engagement with prevention and treatment services [38-40]. Moreover, because of substantial differences in pharmacological properties, patterns of risk behaviours [41-43] and the availability of pharmacological treatment options only for opioid dependence, [44, 45] we expect a higher all-cause mortality rate among stimulant users, but higher drug-related mortality among opioid users. Finally, we anticipate any detention within correctional services to be associated with greater mortality among PWID[46].

AIMS: Our overall objective is to characterise mortality trends and associated causes in a sample of PWID living in a large, urban Canadian city. Our specific aims (SA) are to:

SA1: Describe overall and cause-specific, sex-stratified and age-adjusted mortality rates among PWID and associated trends over time;

SA2: Estimate associations between primary drug of injection and mortality;

SA3: Estimate associations between recent incarceration, stratified by setting (jail vs prison) and time spent in custody, and mortality.

METHODS:

Study context: This study will leverage data collected as part of St Luc/HEPCO, an ongoing CIHR/FRQS-funded prospective cohort study of PWID in Montreal (1992-). Detailed descriptions of cohort recruitment and follow-up procedures have been published [5, 30]. Briefly, eligibility for recruitment requires drug injection in the past six months and age ≥18 years. In the absence of a sampling frame for PWID, participants are recruited via diverse strategies including word-of-mouth and referrals from community-based programmes and addiction centres.

At baseline and each follow-up visit (scheduled 6-monthly until 2011 and 3-monthly thereafter) venous blood samples are drawn by a trained nurse for HIV and HCV serological testing and socio-demographic, behavioural and service use data are collected via an interviewer-administered questionnaire. Informed consent is obtained at each study visit following a protocol approved by the Institutional Review Board of the CHUM.

Since 1992, we have recruited a total of 4143 PWID (789 (19%) female).

Total participants recruited	1992-1998	1999-2004	2005-2011	2012-2019
4143	2618	539	701	285

Mortality data: Mortality data for the years 1992-2015 (most recent year available) will be obtained via record linkage with the Institut de la Statistique du Québec (ISQ) using participant name, sex, birthdate, and provincial health insurance number as linkage keys. Approval will be sought from the Commission d'Accès à l'Information (CAI), the provincial agency granting authorization for use of linked databases. The ISQ codes cause of death using the International Classification of Diseases Revision 9 (1992-1999) and 10 (2000-2015). Primary (1992-2015) and secondary (2000-2015) causes are provided [47] and will be classified into pre-defined categories based on bridge-coding studies, [48-50] prior research, [1, 2] and input from applicants experienced in mortality research (SL, NK). We are currently seeking ethical approval for data linkage through the CHUM Institutional Review Board.

Exposure variables (SA2 and SA3): The St Luc/HEPCO questionnaire elicits detailed information on the types of drugs consumed, modes (injected, smoked, snorted) and frequency of administration, incarceration patterns, and other variables relevant to the health of PWID, including markers of socioeconomic disadvantage such as unstable housing and income. Updated at each visit, these data permit a refined assessment of injection drug use (SA2) and incarceration (SA3) patterns in relation to mortality, while adjusting for potential confounders.

SA2: Based on the types of injected drugs reported by participants and the frequency of injection for each type (i.e., total no. of injections in the previous three months), we will classify the variable "primary drug injected" as either cocaine, amphetamine, heroin or other opioids (primarily prescription opioids).

SA3: Incarceration patterns will be examined according to (i) any detention in the prior three months, and (ii) detention stratified by the setting (local jail, provincial or federal prison) and by the time spent in custody (≤1 week, >1 week and ≤ 1 month, and >1 month, consistent with definitions used by Statistics Canada [24]).

Age, duration of injection, housing and income stability, opioid agonist treatment and other potentially relevant confounders will be considered in the analyses, following in-depth examination of the literature.

Feasibility: Co-applicants on this proposal have made landmark contributions to HCV/HIV and addiction research, presenting a team with expertise spanning epidemiology, public health, and clinical research. Throughout her career, JB (PI) has contributed to a better understanding of factors impeding and facilitating HIV and HCV prevention efforts,[5, 29, 51-54] documenting the effect of HIV/HCV testing,[53, 55, 56] harm reduction services,[5, 57-59] and clinical care [60-62] on risk behaviors and viral outcomes among PWID. DJA has complementary expertise in research related to substance abuse, mental health and HCV [63-67], and together with JB, currently co-leads the St Luc/HEPCO cohort as well as several multisite RCTs testing novel models of care for HCV/HIV (NIDA-funded NCT03981445) and opioid misuse (CRISM-funded OPTIMA trial). Other co-applicants bring expertise in the study of PWID mortality and prisoner health. SL, newly recruited to CRCHUM, has published widely on mortality in PWID, including trends over time in all-cause and cause-specific deaths [68-71] and the role of incarceration and release from prison on mortality rates [71-75]. NK designs, deploys and evaluates evidence-based models of care in Canadian prison settings to improve engagement along the HIV/HCV care cascades for incarcerated and released inmates [76-78], and is Vice-Chair of the International Prisons HCV Network. She has also examined mortality trends among HIV/HCV co-infected populations in Canada [79]. AAA and SH are post-doctoral fellows specialised in the epidemiology of drug use and related harms, including HCV transmission [10, 33, 80], suicide [64, 65], and healthcare

access for PWID [31, 33, 81, 82]. Experienced in longitudinal biostatistics, these young researchers will take a lead role in design, analysis and reporting on this project. More broadly, the St Luc/HEPCO cohort is already integrated within the Réseau SIDA-MI and has the necessary physical and human capital to ensure the success of this research. Based at the CRCHUM, this includes office space and information technologies as well as salary support for research coordination, data cleaning and management, and statistical support from a senior statistician.

Anticipated challenged and solutions: First, we recognise that provincial approvals for administrative data linkage are often subject to significant delays. The CAI has recently introduced an online *Guichet d'accès aux données de recherche* intended to simplify and streamline this process, and we predict a six-month wait for the mortality data. However, it is possible that this could take up to a year. To minimise delays, we will prepare this application immediately, ready for submission upon receipt of ethics approval. Second, examination of mortality trends over long periods is challenged by changes in classification and coding of causes of death (e.g. from ICD 9 to 10). Though approximate equivalences have been identified for research purposes[48-50], we will exercise caution in analysis and interpretation. Third, though record linkage is an optimal method of identifying mortality among cohort participants, misclassification cannot be ruled out. For instance, we may fail to identify some individuals in the ISQ database due to insufficient/incorrect identifying information, leading to underestimation of mortality rates. We expect the impact to be small, however, particularly given the extensive retracing efforts in place at the cohort. Fourth, loss-to-follow-up will limit the availability of contemporaneous behavioral data for participants who left the cohort some time before their death (e.g., >2 years). Statistical techniques for missing data (e.g. multiple imputation) or censoring will be used to address this, as appropriate. Fifth, misclassification of self-reported data is possible, however the recent reference frame of interview questions (i.e., past-month or past three months) minimizes the risk of recall errors. Finally, our sample may not be representative of all PWID in Montréal. However, a history of extensive recruitment in the community through different avenues (word of mouth, shelters, food banks) and addiction treatment program enhances the generalizability of findings.

ANALYSES AND ANTICIPATED RESULTS: Given sex/gender-based differences in mortality among PWID [1], all analyses will be stratified by sex. Overall and cause-specific crude mortality rates and associated 95% confidence intervals will be estimated using the Poisson distribution. To determine whether overall and cause-specific rates of death have changed over time, we will fit age-adjusted Poisson regression models with calendar time as the primary independent variable. To identify excess mortality burden compared with the general population, we will estimate standardized mortality ratios using death rates in an age-matched Quebec population from provincial mortality statistics. Associations between drug use/incarceration patterns and mortality will be examined using Cox regression and competing risk models [83, 84]. Anticipated results are in line with hypotheses.

TIMELINE

Period starting…	2020-01	2020-04	2020-07	2020-10	2021-01	2021-04	2021-07	2021-10
Obtain ethical approval from the CHUM IRB								
Submit data request to Commission d'accès à l'information								
Literature review and drafting of study concepts, designs								
Development of mortality classification schemes								
Receive ISQ mortality data*								
Analysis and writing								

* Expected timelines are not provided by the CAI and it is possible that this will take up to a year.

CONCLUSION AND RELEVANCE: Since 1992, the St Luc/HEPCO cohort has served to improve our understanding of the health and behaviour of PWID in Montréal. Capitalising on decades of community-based recruitment and interviewing, this funding will secure the data needed to expand its relevance and impact. Adding mortality data to the cohort will foster new collaborations and a new agenda of prevention research within the network. It will provide essential statistics and trends related to the risk and causes of death among PWID and enable future studies to model the likely impact of interventions to reduce premature mortality. For instance, the data can inform mathematical models underpinning local initiatives such as *Montreal Sans Hep C*, a micro-elimination program led by researchers from the network (M Klein, C Greenaway and JB) that requires comprehensive epidemiologic data to plan, monitor, and demonstrate achievement of reductions in HCV-related mortality.

BUDGET & JUSTIFICATION

A total budget of **$30 000** is requested for this project. This includes:

- **$5 000** for the cost of record linkage
  This sum is requested in order to link mortality data from the Institut de la Statistique du Québec (ISQ) to the St Luc / HEPCO database. The cost estimate was provided by the ISQ based on a sample size of 3500* participants and a linkage period of 1992 to 2015. It includes linkage of data related to causes of death (including primary and secondary cases, coroners' notification, autopsy information), place of death, and evidence of a reportable disease (whether related to the death or not).

  ** An initial triage will be conducted within the St Luc/HEPCO database to identify participants for data linkage (e.g., those who did not come back for a follow-up visit).*

- **$25 000** to cover one year of stipend support for a doctoral student
  This sum is requested to fund a PhD student who will undertake research activities related to the project, such as obtaining ethics approvals, conducting literature searches and data analysis, and writing manuscripts.

Research coordination and statistical support from a senior statistician with experience in working with the St Luc/HEPCO Cohort database will be provided in-kind by the cohort. Similarly, office space and information technologies (computer workstations, printing and teleconferencing, data storage etc.) will be available in-kind through the St Luc/HEPCO cohort and the CRCHUM.

This pilot funding will initiate a new research agenda for the cohort, which has historically focused on the prevention and natural history of HIV and HCV infection among PWID. It is a cost-effective means to add substantial value to this longstanding study, and new partnerships developed in this initial phase will concretise and ensure the longevity of this endeavour. The investigation of mortality is a natural next step for the cohort, and the relatively low cost of obtaining these data means that we will be able to update them at regular intervals. Combined with new expertise in the study of mortality and prisoner health, this presents the opportunity for a sustainable and impactful program of research.

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Réseau SIDA/MI

CRITÈRES DE SÉLECTION - BRUNEAU – 24

Modèle des Instituts de recherche en santé du Canada / IRSC			
	Impact potentiel	**Intervalle**	**Mérite scientifique**
Subventionnable	Extrêmement important	4,5 – 4,9	Exceptionnel
	Très important	4,0 – 4,4	Excellent
	Important	3,5 – 3,9	Excellent, mais peut nécessiter une révision
Non subventionnable	Modéré	3,0 – 3,4	Très bien, mais nécessite une révision pour être subventionnable
	Limité	2,5 – 2,9	Révision importante nécessaire
	Négligeable	0,0 – 2,4	Laisse beaucoup à désirer

Il est proposé aux évaluateurs d'accorder une note (0,0 à 4,9) pour chacun des critères, en vue de les additionner et de les diviser par 5.

1. RATIONNEL *(1.1 Mise en contexte et* *1.2 importance de l'étude proposée)*	*4.3*
2. HYPOTHÈSE *(Veuillez énoncer clairement* *2.1 l'hypothèse principale du projet et* *2.2 les hypothèses secondaires, le cas échéant).*	*4.4*
3. OBJECTIFS *(Veuillez spécifier* *3.1 les objectifs principaux, et* *3.2 les objectifs secondaires, le cas échéant).*	*4.4*
4. MÉTHODOLOGIE *(Veuillez spécifier* *4.1 si des outils ou des méthodologies innovantes seront utilisées,* *4.2 Veuillez préciser la faisabilité,* *4.3 les difficultés potentielles et* *4.4 les mesures d'atténuation, lorsque pertinent)*	*4.4*
5. ANALYSES ET RÉSULTATS ANTICIPÉS *(Veuillez préciser* *5.1 les méthodes statistiques qui seront utilisées* *5.2 et énoncer les résultats attendus).*	*3.5*
6. ÉCHÉANCIER *(Veuillez identifier* *6.1 tapes à suivre pour l'atteinte des objectifs.)*	*4*

Réseau SIDA/MI

Bruneau - 2a

Modèle des Instituts de recherche en santé du Canada / IRSC			
	Impact potentiel	**Intervalle**	**Mérite scientifique**
NOM DU PARTICIPANT : BRUNEAU			**TOTAL** = 4.1
FORCES : PROJET TRÈS BIEN ÉCRIT, LE RATIONNEL ET LES HYPOTHÈSES SONT TRÈS PERTINENTES, LA DISPONIBILITÉ DE COHORTES D'USAGERS DE DROGUE EST UNE OPPORTUNITÉ TRÈS INTÉRESSANTE POUR MENER CETTE RECHERCHE QUI PERMETTRA SI LES HYPOTHÈSES SONT VÉRIFIÉES DE MIEUX RÉFLÉCHIR AUX POLITIQUES DES DROGUES EN TERMES DE CONSÉQUENCES SANITAIRES. L'ÉQUIPE A BEAUCOUP D'EXPÉRIENCE SUR LE SUJET. LE PLAN D'ANALYSE EST BIEN DÉTAILLÉ ET LES VARIABLES SONT DÉCRITES AVEC SOIN. LES DIFFICULTÉS SONT BIEN ANTICIPÉES EN PARTICULIER POUR L'OBTENTION DES DONNÉES DE LA BASE DES DÉCÈS.			
FAIBLESSES : LE MODÈLE DE POISSON POUR DÉTERMINER LES ÉVOLUTIONS DE LA MORTALITÉ ET DE SES CAUSES POSE QUESTION : POUR TESTER LES TENDANCES LINÉAIRES DANS LES INCIDENCES CALCULÉES SUR DIFFÉRENTES PÉRIODES CALENDAIRES, ON DEVRAIT MODÉLISER LA VARIABLE DÉPENDANTE "TAUX D'INCIDENCE" (QUI EST CONTINUE - DU COUP ON UTILISE UN MODÈLE DE RÉGRESSION LINÉAIRE) EN FONCTION DE LA VARIABLE EXPLICATIVE "ANNÉE CALENDAIRE"			

Réseau SIDA/MI

CRITÈRES DE SÉLECTION - BRUNEAU – 26.

Modèle des Instituts de recherche en santé du Canada / IRSC			
	Impact potentiel	**Intervalle**	**Mérite scientifique**
Subventionnable	Extrêmement important	4,5 – 4,9	Exceptionnel
	Très important	4,0 – 4,4	Excellent
	Important	3,5 – 3,9	Excellent, mais peut nécessiter une révision
Non subventionnable	Modéré	3,0 – 3,4	Très bien, mais nécessite une révision pour être subventionnable
	Limité	2,5 – 2,9	Révision importante nécessaire
	Négligeable	0,0 – 2,4	Laisse beaucoup à désirer

Il est proposé aux évaluateurs d'accorder une note (0,0 à 4,9) pour chacun des critères, en vue de les additionner et de les diviser par 5.

1. RATIONNEL *(1.1 Mise en contexte et* *1.2 importance de l'étude proposée)*	• Project proposes to characterize mortality rates, trends and determinants among PWID in Montreal, Canada • Evidence in Canada is limited and has been limited to the Vancouver context • Data are needed to design effective interventions to reduce mortality among PWID • Issue appears exacerbated by the opioid crisis • There is limited evidence on the relationship between incarceration and mortality among PWID in Canada • There is a substantial literature to support the proposed work • **Score: 4.5**
2. HYPOTHÈSE *(Veuillez énoncer clairement* *2.1 l'hypothèse principale du projet et* *2.2 les hypothèses secondaires, le cas échéant).*	• Age and sex-standardized mortality rates expected to be much higher among PWID relative to the general population; increased mortality also expected in women, stimulant users and previously incarcerated individuals • **Score: 4.2**
3. OBJECTIFS *(Veuillez spécifier* *3.1 les objectifs principaux, et* *3.2 les objectifs secondaires, le cas échéant).*	• Overall objective is to characterize mortality trends and associated causes in PWID in Montreal, Canada • Three clear complementary specific aims are proposed • **Score: 4.2**
4. MÉTHODOLOGIE *(Veuillez spécifier* *4.1 si des outils ou des méthodologies innovantes seront utilisées,* *4.2 Veuillez préciser la faisabilité,*	• Study will use data collected as part of ongoing PWID cohort in Montreal, Canada • Cohort has been well-characterized with respect to demographic and socio-behavioral characteristics

Réseau SIDA/MI

Bruneau - JB

Modèle des Instituts de recherche en santé du Canada / IRSC			
	Impact potentiel	**Intervalle**	**Mérite scientifique**
4.3 les difficultés potentielles et *4.4 les mesures d'atténuation, lorsque pertinent)*			• Mortality data are available and IRB approval to use linked data will be obtained, although possible delays are expected and misclassifications are possible • Exposure variables have been thoroughly presented; some of these variables rely on self-report – it would be helpful to know steps to reduce bias • PWID cohort has experienced some loss-to-follow-up which may lead to bias; mitigation strategy includes statistical techniques for missing data • Strong case for feasibility within the funding period • **Score: 4.0**
5. ANALYSES ET RÉSULTATS ANTICIPÉS *(Veuillez préciser* *5.1 les méthodes statistiques qui seront utilisées* *5.2 et énoncer les résultats attendus).*			• Proposed analyses are thoroughly described and will account for sex-based differences • Poisson regression, Cox regression and competing risk models will be employed and are aligned with proposed hypotheses and study objectives • **Score: 4.2**
6. ÉCHÉANCIER *(Veuillez identifier* *6.1 les étapes à suivre pour l'atteinte des objectifs.)*			• Proposed timeline clearly presented with possible delay in receiving mortality data • **Score: 4.0**
NOM DU PARTICIPANT : BRUNEAU			**TOTAL = 4.18**

FORCES :

- Principal Investigator has wealth of experience in areas of HCV/injecting drug use and co-applicants have made landmark contributions to HIV/HCV and addiction research and have complementary expertise (epidemiology, public health and clinical research)
- Team has established cohort of > 4,000 PWID in Montreal
- Project will capitalize on decades of community-based recruitment, has important public health significance for PWID in Montreal, Canada and may lead to important interventions to reduce premature mortality
- Budget and justification appear reasonable in light of the proposed objectives
- Project will add value and represents a natural next step for the PWID cohort

FAIBLESSES :

- Possible delays expected in obtaining mortality data and use of self-reports for some of the measures

Réseau SIDA/MI

CRITÈRES DE SÉLECTION - BRUNEAU - JC

Modèle des Instituts de recherche en santé du Canada / IRSC			
	Impact potentiel	**Intervalle**	**Mérite scientifique**
Subventionnable	Extrêmement important	4,5 – 4,9	Exceptionnel
	Très important	4,0 – 4,4	Excellent
	Important	3,5 – 3,9	Excellent, mais peut nécessiter une révision
Non subventionnable	Modéré	3,0 – 3,4	Très bien, mais nécessite une révision pour être subventionnable
	Limité	2,5 – 2,9	Révision importante nécessaire
	Négligeable	0,0 – 2,4	Laisse beaucoup à désirer

Il est proposé aux évaluateurs d'accorder une note (0,0 à 4,9) pour chacun des critères, en vue de les additionner et de les diviser par 5.

1. RATIONNEL *(1.1 Mise en contexte et* *1.2 importance de l'étude proposée)*	4.5
2. HYPOTHÈSE (Veuillez énoncer clairement 2.1 l'hypothèse principale du projet et 2.2 les hypothèses secondaires, le cas échéant).	4.5
3. OBJECTIFS (Veuillez spécifier 3.1 les objectifs principaux, et 3.2 les objectifs secondaires, le cas échéant).	4.5
4. MÉTHODOLOGIE (Veuillez spécifier 4.1 si des outils ou des méthodologies innovantes seront utilisées, 4.2 Veuillez préciser la faisabilité, 4.3 les difficultés potentielles et 4.4 les mesures d'atténuation, lorsque pertinent)	4.5
5. ANALYSES ET RÉSULTATS ANTICIPÉS (Veuillez préciser 5.1 les méthodes statistiques qui seront utilisées 5.2 et énoncer les résultats attendus).	4.5
6. ÉCHÉANCIER (Veuillez identifier 6.1 les étapes à suivre pour l'atteinte des objectifs.)	4.5

Réseau SIDA/MI

Bruneau - 2c

Modèle des Instituts de recherche en santé du Canada / IRSC			
	Impact potentiel	**Intervalle**	**Mérite scientifique**
NOM DU PARTICIPANT : BRUNEAU			**TOTAL** = 27 = 4.50
FORCES : TRÈS BON PROJET, INTÉRESSANT ET IMPORTANT. TRÈS BONNE QUALITÉ DU PI ET DES AUTRES MEMBRES DE L'ÉQUIPE AVEC DE TRÈS NOMBREUSES PUBLICATIONS DANS LE DOMAINE DU VIH, DE LA COÏNFECTION ET DE LA PROBLÉMATIQUE DE L'UTILISATION DE DROGUES. L'APPARITION DE NOUVELLES DROGUES COMME LES OPIACÉS EST AUSSI PRISE EN COMPTE DANS CE PROJET. ANALYSE STATISTIQUE APPROPRIÉE			
FAIBLESSES : SANS PRÉCISION SUR LE NOMBRE DE DÉCÈS DÉJÀ OBSERVÉ DANS LA COHORTE DE DONNÉES (N=4143), AVEC DES INDIVIDUS INCLUS DEPUIS 1992, IL EST DIFFICILE DE SAVOIR SI L'ANALYSE STATISTIQUE PERMETTRA DE RÉPONDRE DE FAÇON SATISFAISANTE (AVEC LA PRÉCISION NÉCESSAIRE) À TOUS LES OBJECTIFS DU PROJET.			