Investigating the correlation between ambient air pollution and the use of inhalation therapy: an analysis of INTEGO database: a protocol article

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Abstract

Introduction: Air pollution is an important global problem. Ambient air pollution consists of a mixture of pollutants of which the percentage in the air keeps increasing. Evidence is growing on the impact of ambient air pollution on human health. Air pollution has proven to increase morbidity and mortality mostly cardiopulmonary related, but evidence for the influence on other health aspects is also emerging. Some subgroups prove to be more susceptible to the negative effects of ambient air pollution such as people with comorbidities, low economic class, etc.

Methods: A linked dataset is created starting from the Intego database based on data from general practitioners and a dataset of the Flanders Environment Agency with annual means for all the pollutants. The correlation between higher annual means of ambient air pollution and an increase in use of inhalation medication is examined.

Discussion: We expect to find an increase in inhaler use with chronic exposure to higher levels of ambient air pollution. This research will be used to support local governments to change regulations concerning ambient air pollution. Further research can be conducted on larger scale as well as on harder endpoints.

Conclusion: Ambient air pollution is an important worldwide problem with significant impact on human health. Research should help local governments to make well-informed decisions on how to tackle the air pollution problem.

Abstract Nederlands

Introductie: Luchtvervuiling is een belangrijk en wereldwijd probleem. Luchtvervuiling bestaat uit mengsel van verschillende polluenten van dewelke de hoeveelheid in onze lucht

blijft stijgen. Wetenschappelijk bewijs voor de negatieve impact van luchtvervuiling op de gezondheid is aan het opstapelen. Er is bewijs voor zowel morbiditeit als mortaliteit ter hoogte van het cardiorespiratoir stelsel maar recent komt er ook bewijs voor invloed op andere aspecten van gezondheid. Sommige subgroepen van de bevolking blijken meer gevoelig aan de negatieve effecten van luchtvervuiling, zoals mensen met comorbiditeiten en mensen van lage sociale klasse enzovoort.

Methode: Een gelinkte dataset wordt gemaakt van enerzijds de Integodatabase op basis van informatie van de huisartsen en anderzijds van een dataset van de Vlaamse Milieumaatschappij met jaargemiddelden van de verschillende polluenten. Een correlatie wordt gezocht tussen plaatsen met hogere luchtvervuiling en een hogere hoeveelheid voorgeschreven inhalatie medicatie.

Discussie: We verwachten een stijging te zien van het voorschrijven van inhalatiemedicatie in gebieden waar de niveaus van luchtvervuiling waaraan de mensen worden blootgesteld hoger zijn. Het onderzoek zal bijdragen in de verdere aanpak van luchtvervuiling door de regering. Verder onderzoek is zeker nodig, er kan zeker nog gekeken worden naar et effect van stijging van luchtvervuiling op korte termijn zoals in periodes van smog. Ook zou, zeker in Europa, deze studies ook moeten gebeuren op grotere schaal, over de landsgrenzen heen. Ook de correlatie met hardere eindpunten zoals mortaliteit en hospitalisaties moeten onderzocht worden.

Conclusie: Luchtvervuiling is een belangrijk en wereldwijd probleem met een significante impact op de gezondheid van de mens. Ons onderzoek, alsook verder onderzoek rond luchtvervuiling, moet vooral de beleidsmakers helpen om goed geïnformeerde beslissingen te nemen rond de aanpak van luchtvervuiling.

Abbreviations

GINA: Global Initiative for Asthma

GP: General Practitioner

ICD-10: International Statistical Classification of Diseases and Related Health Problems, 10th edition

ICPC-2: International Classification of Primary Care, 2nd edition

IFDM: Immission Frequency Distribution Model

OSPM: Operational Street Pollution Model

PM: Particulate matter

$PM_{2,5}$: Particulate matter with a median diameter <2,5µm

PM_{10}: Particulate matter with a median diameter <10µm

RIO: Residual Interpolation optimised for Ozone

VMM: Vlaamse Milieu Maatschappij (Flanders Environment Agency)

WHO: World Health Organization

Key words

Ambient air pollution

Inhalation therapy

Inhaler

Background

"It has come to my attention, that air pollution is polluting the air!" George W. Bush once said. Luckily we have learned more today! Air pollution is these days a well-known global issue. Estimations show that up to 90% of the people in the world breathe air that does not comply with the WHO Air Quality Guidelines. (1) Differentiation can be made between indoor and outdoor air pollution given they are produced by different sources and thus have a different composition. In this research there is solely the focus on ambient, or outdoor, air pollution. The main sources of outdoor air pollution include vehicle exhaust, industrial emissions, agriculture etcetera. (1, 2) Ambient air pollution consists of a mixture of particles, gases and metals. The most researched component is particulate matter (PM). It consists of a mixture of solid and liquid particles of different sizes that remain suspended in the air, including: sulfates, nitrates, ammonia, sodium chloride, black carbon, mineral dust and water. (1, 2) We can divide this particulate matter in different subgroups being PM10, PM2,5 and ultrafine particulates. PM10 or respirable particulate matter are particulates with an aerodynamic diameter <10µm. PM10 is widely researched because particle of 10µm and less are the most health-damaging. The smaller the size of the particles the deeper they can penetrate into the lungs and the more they can be absorbed into the blood circulation. PM2,5 is a mixture of particles that have an aerodynamic diameter of <2,5µm and might now be seen as a more important indicator for health risk due to air pollution than PM10. They are mainly formed from gasses. Lastly there are ultrafine particles which are formed by nucleation, the initial stage of the process by which a gas transforms to a particle. They can be up to 1µm in size but are mostly only a few nanometers in size.(1, 3) According to the latest report of the World Health Organization (WHO) on ambient air pollution, the mean $PM_{2,5}$ concentrations still globally increased by 8% in the period of 2008 until 2013. This increase was most prominent in middle- and low-income WHO-regions. (1)

The negative effect outdoor air pollution has on human health, has already been proven repeatedly. The finest particles are able to penetrate deepest into the lungs and even the bloodstream, so thereby have a greater potential to be harmful, whereas bigger particles will deposit in nasopharynx and trachea. The finest particles included in ambient air pollution are $PM_{2,5}$. The exact mechanisms through which outdoor air pollution causes these adverse effects are totally known but systemic inflammation and oxidative stress are definitely included. According to this pathomechanisms a great variety of health issues associated with outdoor air pollution can be expected. (2-4) In addition to particulate matter also nitrogen oxides and ozone have proven negative impacts on health. (1, 4)

Air pollution is known to increase morbidity and mortality. The latest report of the World Health Organization (WHO) also stated that in 2012, 1 out of 9 deaths could be attributed to outdoor air pollution. Globally this accounted for 3 million deaths associated with outdoor air pollution in 2012. (1) Apart from causing mortality, numerous acute and chronic diseases are also caused or worsened by outdoor air pollution. Most of the health risks caused by $PM_{2,5}$ are associated with the cardiopulmonary system. In the cardiovascular system $PM_{2,5}$ concentration has proven to be an independent risk factor for stroke and ischemic heart diseases. For the respiratory system there is a correlation between $PM_{2,5}$ concentration and lower respiratory tract infections, chronic obstructive pulmonary diseases, asthma and lung cancer. Also, there is evidence for a correlation between $PM_{2,5}$ and pre-term birth, low birthweight and infant or fetal death. As a result of all these correlations outdoor air pollution is the largest environmental risk factor for health problems. (1-4)

However, evidence has shown that not every person is evenly susceptible to the negative effects of ambient air pollution. People with pre-existing medical conditions, such as chronic cardiorespiratory diseases, pneumonia and type 2 diabetes, are more likely admitted to hospital or are more likely to die. Besides from diseases, young children, low economic class

and poor education have shown to be risk factors to be more susceptible to outdoor air pollution. (3)

In this research the correlation between outdoor air pollution and respiratory morbidity is addressed. Specifically, the correlation between long-term exposure to ambient air pollution and the use of inhalation therapy as a proxy for severity of respiratory morbidity was investigated. Hereby the different susceptibility of subgroups of the population, being low economic class, sex and age, are investigated. With this investigation the impact of ambient air pollution on the respiratory health in Flemish people is assessed by using the increase in the use of inhalers as a parameter for respiratory complaints.

Methods

Intego database

The investigation of our hypothesis is executed on a linked database based on the existing Flemish Intego-database. The Intego-database exists since 1994 and gathers its information from the Flemish general practitioners (GP). The 2018 Intego-database contains information of 268 GP's spread over 88 practices throughout Flanders. The database contains coded and dated morbidity data, demographic data (age, sex, socio-economic status,…), coded and dated prescribed medication, dated lab results, clinical parameters, vaccinations, etc. Diagnoses are coded by an international classification system used in epidemiological studies such as ICP-2 and ICD-10. Thus the Intego database represents an open cohort study in which every year persons leave and enter. By correcting data from Intego for the section of the population that doesn't consult a GP on a yearly basis, an extrapolation to the entire Flemish population can be made.

Data collection

Data are collected through a trusted third party. Since 1/1/2019 data are collected by eHealth and sent through eHBox codage to the Healthdata datawarehouse. The whole mode of operation of Health data is described by Delvaux et al (5). Home address information received from the general practitioners is generally correct because it is received by reading the patients eID-card. The coded address information is then sent to VITO and there converted into geographical coordinates. These coordinates are linked to a certain environmental burden which then are linked to the patient in question. The linked patient and environmental data are then returned to Healthdata (fig 1). Patients have the option to choose for an opt-out resulting in their data not being sent to the database. All data also have to meet the quality requirements being: an average of 1 diagnosis per patient per year, a minimum of 95% correctly coded diagnoses and both these parameters have to be stable throughout 3 year.

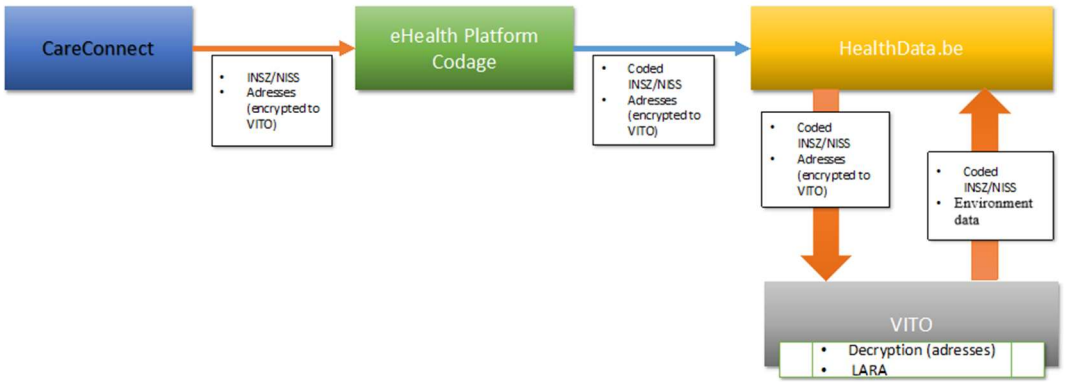

Fig. 1 Dataflow of patient information and linking of patient information with environmental information.

The linked dataset

The Intego dataset is linked with a dataset concerning ambient air pollution. The address available in the Intego database is converted into coordinates and then linked with the corresponding air pollution parameters. This second dataset concerning ambient air pollution

is retrieved from the Flemish environment cooperation (VMM). It contains annual mean values for $PM_{2,5}$, PM_{10}, O_3, NO_2 and Black Carbon. This dataset is primarily based on measurements throughout Flanders. Because it is impossible to measure air quality everywhere in Flanders the ATMO-street is used. It is a linking of 3 models that estimate air quality. First there is the RIO interpolation model that estimates air quality based on automatic air quality measurements and land utilization (example given: cultivation versus forestation). In this manner the RIO model produces a background concentration of air pollutants for an area of 4x4 km^2. This model is linked to the IFDM, which is a model that calculates the emission of point- and linesources from emissiondata and how they influence the air quality in their surroundings. This includes for example road traffic and industrial buildings. The IFDM also corrects for meteorological measurements of wind and temperature because they influence the distribution of ambient air pollution and velocity of chemical reactions in the air. A correction for duplication of the measurements is also incorporated because part of these emissions are also registered by RIO's interpolated measurements. By linking these two models a more detailed image of air quality can be given on a scale of 10x10m^2. Finally this is linked to the OSP-model that gives detailed information of the street configuration. It calculates the impact of street canyoning hence narrow streets are less ventilated, the ambient air pollution thither is less diluted. (6, 7)
These models for air quality estimation are extensively validated.(8-10)

Study objectives

In this linked dataset correlations are investigated between environmental risk factors and health outcome factors. In this study protocol there is a focus on the correlation between chronic exposure to ambient air pollution and the use of inhalers. In table 1 in the appendix all inhalation medication, registered for use in Belgium, are listed as substance and their

corresponding brand names. It includes both short- and long-acting substances and either bèta-2-mimetica as anticholinergics as corticosteroids and all their possible combinations as well. This exhaustive list is used to search for inhalation medication prescriptions in the Intego database.

The selection of the parameters representing ambient air pollution is based on the available literature. Parameters with the most evidence for having a substantial impact on human health are chosen. Also there is taken into account for which parameters there are adequate measurements/calculations available in Flanders. Eventually PM_{10}, $PM_{2,5}$, SO_2 and NO_2 are selected as parameters representing ambient air pollution. The effect of chronic exposure to these components on health are assessed. The annual means for each component, retrieved from the ATMO-street model, are used as chronic exposure to ambient air pollution. The effect of all these component together will be assessed hence they are normally breathed in as a mixture. Also a stratification will be done to assess the impact of each individual component on the human health.

The data are corrected for the influences of age, sex, tobacco use and social status. Data for age, sex and smoking are available in the Intego database. Data for social status are deducted from the information from the health insurance fund available in the Intego database. Furthermore subgroup analysis is performed to investigate whether some subgroups are more susceptible to ambient air pollution. Subgroups were created by sex, age: ≥65 years or children 0-18 years, low social status and patients with chronic respiratory or cardiac diseases.

We have to report some difficulties during the data collection of the data concerning the general practices. The gathering of these data was not included in this thesis. Due to these problems the linked dataset was not available for analysis in the time frame set for this thesis.

Discussion

Result expectations

With this study we expect to find a larger amount of prescriptions of inhalation medication in areas where there is a larger burden of ambient air pollution. If there is an increase in prescriptions it can be seen as a decrease of respiratory health and evidence that ambient air pollution is a burden of respiratory morbidity. An increase in prescriptions for short-acting substances will display an increase in morbidity in earlier healthy people and an increase in less disease control in people who already have a morbidity. An increase in prescriptions for long-acting substances and corticosteroids reveals more progression of morbidity which results in a step-up in therapy. Though a remark must be made. Since the new GINA guidelines some LABA + corticosteroids associations are used as rescue medication and could also indicate less disease control.

Strengths and limitations

The general practice-based dataset contains information of patients of 268 general practitioners throughout Flanders. In 2016 this represented 2% of the Flemish population, now it will be even more. If these data are corrected for the part of the population that does not visit a general practitioner yearly, these findings can be extrapolated from this dataset to the whole Flemish population. The construction of this dataset allows us to follow larger groups of patients over a longer period of time, what makes it ideal for this sort of epidemiological studies. There are also a number of quality requirements the data have to fulfill in order to make the data more reliable. There also has to be noted that no data from specialists are available. There is certainly a part of the population that retrieves their prescriptions for inhalation medication from their pneumologist. Considering the health care

structure in Belgium, this is believed to be a minor part of the population.

Concerning the ATMO-street model there are also a few limitation. Ideally there are performed measurements everywhere throughout Flanders but practically this is not possible. The ATMO-street model is validated as an accurate estimation model for ambient air pollution but it remains an estimation and could differ from the real life values. Also there are known limitations inherent to the ATMO-street model. There are no data on smaller traffic routes, for those smaller routes only data from RIO are available. The emission of traffic on a certain route is also an estimation based on traffic counts and speed limits. Temporary changes caused by for instance traffic jams or traffic diversions are not accounted for. Also the effects of trees in streets and the kicking up of dust in street canyons are not taken into account. Local emission from indoor air pollution or agriculture are also not incorporated in this model. All these limitations taken into account ATMO-street model still gives us a very detailed representation of air quality in Flanders. (6, 7)

Ambient air pollution is known to be a complex mixture of which the composition can vary through different locations. We are exposed to air pollution as a mixture of all these individual pollutants. The effect of ambient air pollution on our health can't be reduced to the sum of the effects of the individual pollutants. To know the true and total impact of ambient air pollution multi-pollutant models are necessary. (11)

Also the important influence of indoor air pollution is not taken into account here. It has a significant adverse effect on our health on itself but it also contributes to ambient air pollution when discharged from our homes. In the used models for ambient air pollution the influence of indoor air pollution is not included.

Implications

Since these results can prove an increase in morbidity related to ambient air pollution in Flanders it will show our governors the importance of containing ambient air pollution. In this manner they can make more well-informed policy choices. Stratification from our results for different pollutants will give an idea which pollutants are more harmful for respiratory health and more resources can go out to diminish these particular pollutants.

It should also be noted that a substantial part of the inhalation devices used to administer this medication contain propellants. Currently hydrofluorocarbons is used for this. Although hydrofluorocarbons don't have such a negative impact on the ozone-layer as their predecessor chlorofluorocarbon, they also have a negative impact on global warming. It is proven that they have a substantial carbon footprint (12). Therefore the increase in use of inhalers due to ambient air pollution increases in its turn ambient air pollution.

Further research possibilities

There has to be noted that Flanders is a rather small area in Europe and of course the pollution does not stop at our borders. Since ambient air pollution and climate changes are a rather global matter this problem should also be evaluated on a greater level. Databases throughout the Benelux and Europe should be created to study the problem of ambient air pollution on a greater level since measurements to contain this problem will also be more effective if taken on larger scale.

On the same databases research with different endpoints can be conducted. In this research there is chosen a soft endpoint as an indicator for morbidity. But important research on hard endpoint such as mortality, hospital admissions, etc. should be conducted.

Furthermore suggestions can be made to investigate the effect of short term exposure of higher levels of ambient air pollution. Is there more cardiorespiratory morbidity and mortality in periods of higher ambient air pollution levels?

Conclusion

Ambient air pollution is already a well-known worldwide problem. Evidence is accumulating that ambient air pollution has a significant impact on human health. It has impact on morbidity as well as mortality mostly cardiorespiratory but recent research suggests that also other systems could be affected. This research will help local governments to make well-informed decisions in taking measurements on lowering ambient air pollution.

Declarations

Ethics approval was received from the ethics committee of the KU Leuven university hospital. No further acknowledgements for funding or competing interests are present. The general practice-based dataset analyzed during the current study are available at the Academic Centre of General Practice at the KU Leuven University. Datasets on ambient air pollution in Flanders used in this study are available at the VMM, https://www.vmm.be/data.

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Appendix

Table 1	
Inhallatiemedicatie - stoffen	**Inhalatiemedicatie - producten**
Salbutamol	Airomir
	Novolizer Salbutamol
	Ventolin
Formoterol	Foradil
	Formagal
	Formoair
	Novolizer Formoterol
	Oxis
Indacaterol	Onbrez
Olodaterol	Striverdi
Salmeterol	Serevent
Ipratropium	Atrovent
Aclidinium	Bretaris
Glycopyrronium	Seebri
Tiotropium	Spiriva
	Srivasso
Umeclidinium	Incruse
ipratropium bromide 0,5mg + Salbutamol 2,5mg /2,5ml	Combivent
ipratropium bromide 20µg + fenoterol hydrobromide 50µg	Duovent
ipratropium bromide 0,5mg + Salbutamol 2,5mg /2,5ml	Nebu-iprasal
umeclidinium 55µg + vilanterol 22µg	Anoro
Aclidinium 343µg + Formoterol furamaat 12µg	Duaklir
Tiotropium 2,5µg + olodaterol 2,5µg	Spiolto
Indacaterol 85µg + Glycopyrronium 43µg	Ultibro
tiotropium 2,5µg + olodaterol 2,5µg	Yanimo
Beclometason	Beclophar
Beclometason	Qvar
Budesonide	Budesonid Sandoz
	Budesonide
	Budesonide EG
	Budesonide Teva
	Miflonide
	Novolizer Budesonide
	Pulmicort
Fluticason	Flixotide
budesonide 160µg + Formoterol 4,5µg	Airbufo
Salmeterol 25µg + fluticason propionaat 125µg	Airfusal
budesonide 160µg + Formoterol 4,5µg	Bufomix
Salmeterol 50µg + fluticason propionaat 250µg	Flusalio
Fluticason propionaat 50µg + Formoterol fumaraat 5µg	Flutiform
Salmeterol 25µg + fluticason proprionaat	Flutisacombo

fluticason propionaat + salmeterol 50µg	Flutisamix
Beclometason dipropionaat + Formoterol fumaraat	Inuvair
fluticason furoaat + vilanterol	Relvar
Salmeterol 25µg + fluticason propionaat	Seretide
budesonide + Formoterol	Symbicort
budesonide + salmeterol 20µg	Zephirus
beclometason dipropionaat 87µg + Formoterol fumaraat 5µg + glycopyrronium 9µg	Trimbow
fluticason furoaat 92µg + umeclidinium 55µg + vilanterol 22µg	Trelegy

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S62682		

Surveillance van milieu-gerelateerde ziekten en gezondheidsparameters in Vlaanderen

Geachte Collega

De Ethische Commissie Onderzoek UZ/KU Leuven heeft vermeld protocol onderzocht en besproken op haar vergadering van 8 april 2019.

De EC heeft geen bezwaar tegen het project mits vertrouwelijke behandeling van de gegevens en naleving van de Belgische wetgeving omtrent privacy.

De EC wenst de hoofdonderzoeker/promotor van de studie te wijzen op zijn/haar verantwoordelijkheid betreft de privacy van de persoons-/patiëntgegevens bij contact met de patiënt en/of inzage in het elektronisch medisch dossier, inclusief de correcte implementatie hiervan door medewerkers en studenten. de EC verwijst naar de richtlijnen van ICH/GCP hierover op de website, en benadrukt dat een GCP-opleiding van elke hoofdonderzoeker verwacht wordt. De EC verwijst tevens naar de EU Verordening 2016/679 (Algemene Verordening Gegevensbescherming inzake de bescherming van persoonsgegevens) en de Belgische Wet van 22/8/2002 betreffende de rechten van de patiënt.

Dit project valt niet onder het toepassingsgebied van de wet van 7/5/2004.

De EC gaat ervan uit dat de dienstra(a)d(en)/diensthoofd(en)/zorgprogramma vooraf geïnformeerd zijn en akkoord gaan met de uitvoering van de studie.

Bij het beoordelen van dit dossier werd rekening gehouden met de documenten en informatie gerelateerd aan deze studie, ingediend op 28 maart 2019, 25 april 2019 en 2 mei 2019.

Dit schrijven betreft:

Protocol:
versie 2 dd 02/05/2019
Informatie en toestemmingsformulier:

De EC bevestigt dat ze werkt in overeenstemming met de ICH-GCP principes (International Conference on Harmonization Guidelines on Good Clinical Practice), met de meest recente versie van de Verklaring van Helsinki en met de van toepassing zijnde wetten en regelgeving.

De EC bevestigt dat in geval van belangenconflict, de betrokken leden niet deelnemen aan de besluitvorming omtrent de studie.

Een ledenlijst wordt bijgevoegd.

Aandachtspunten: (indien van toepassing)

De opdrachtgever is verantwoordelijk voor de conformiteit van de anderstalige documenten met de Nederlandstalige documenten.

*Indien er een **Clinical Trial Agreement** is, kan de studie in ons centrum pas aangevat worden wanneer dit Clinical Trial Agreement goedgekeurd en ondertekend is door de gedelegeerde bestuurder van UZ Leuven (en/of desgevallend door bevoegde vertegenwoordiger(s) van KU Leuven Research & Development).*

Studies met geneesmiddelen en sommige studies met "medische hulpmiddelen" dienen door de opdrachtgever aangemeld te worden bij het FAGG.

Studies met geneesmiddelen mogen slechts aanvangen op voorwaarde dat de minister (FAGG) geen bezwaren heeft kenbaar gemaakt binnen de wettelijke termijnen zoals beschreven in art.13 van de Belgische wet van 7/5/2004 inzake experimenten op de menselijke persoon. Voor bepaalde studies met medische hulpmiddelen gelden eveneens wettelijke termijnen (zie KB van 17/3/2009). Voor meer informatie hieromtrent verwijzen we naar de website van het FAGG www.fagg-afmps.be.

Onderzoek op embryo's in vitro valt onder de wet van 11 mei 2003. Voor dergelijk onderzoek is er naast een positief advies van de EC ook een goedkeuring van de Federale Commissie voor medisch en wetenschappelijk onderzoek op embryo's in vitro noodzakelijk vooraleer dit onderzoeksproject kan doorgaan.

Gelieve ook rekening te houden met de regelgeving van het ziekenhuis betreffende weefselbeheer en met de beschikkingen van de wet van 19 december 2008.

Dit gunstig advies van de EC houdt niet in dat zij de verantwoordelijkheid voor de geplande studie op zich neemt. U blijft hiervoor dus zelf verantwoordelijk. Bovendien dient U, als betrokken hoofdonderzoeker, erover te waken dat de resultaten van dit onderzoek correct worden weergegeven in publicaties, rapporten voor de overheid enz..

Gelieve ons mee te delen indien een studie niet wordt aangevat of wanneer ze wordt afgesloten of vroegtijdig onderbroken (met opgave van reden).

Gelieve tenslotte het (vroegtijdige of geplande) stopzetten van een studie binnen de door de wet vastgestelde termijnen mee te delen en binnen het jaar na stopzetting een

Clinical Study Report *aan de EC te bezorgen.*

Graag wensen we er u op attent te maken dat de EC bij een volgende indiening van dezelfde opdrachtgever, verwacht dat er ab initio rekening gehouden wordt met de initiële opmerkingen van de EC.

Met vriendelijke groet,



Prof. Dr. Minne Casteels
Voorzitter
EC Onderzoek UZ/KU Leuven

Ledenlijst/Samenstelling van de Ethische Commissie Onderzoek UZ/KU Leuven op 8 april 2019 (datum van de laatste bespreking van het dossier):

Voorzitter	prof. dr. Maria-Reinhilde Casteels	Clinical Pharmacology
Vice-voorzitter	prof. dr. Dominique Bullens	Paediatrics
	De heer Jean-Jacques Derèze	Medical Legislation
	De heer Kristof Muylaert	Nurse (alternate)
	De heer Mathijs Swaak	Healthy volunteer repres.
	Mevr. Ellen Goetstouwers	Patient representative
	Mevr. Godelieve Goossens	Nurse
	Mevr. Hélène De Somer	Nurse
	Mevr. Katrin Roggeman	Patient representative
	apr. J.R. Thomas	Clinical Pharmacology
	apr. Stefanie Goris	Pharmacist
	dr. José Thomas	Medical Oncology
	dr. Lut De Groote	General Practitioner
	prof. Ben Van Calster	Statistics
	prof. Pascal Borry	Ethics
	prof. dr. Anne Smits	Paediatrics
	prof. dr. Ariel Alonso	Statistics (alternate)
	prof. dr. Benoit Nemery	Pneumology
	prof. dr. Gregor Verhoef	Haematology
	prof. dr. Jan Verhaegen	Laboratory Medicine
	prof. dr. Jan de Hoon	Clinical Pharmacology
	prof. dr. Karin Sipido	Experimental Cardiology
	prof. dr. Maria Schetz	Intensive care
	prof. dr. Simon Brumagne	Physiotherapy
	prof. dr. Xavier Bossuyt	Immunology
	prof. dr. em. Raymond Verhaeghe	Cardiology