

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	International Randomized Controlled Trial evaluating metabolic syndrome in type 2 Diabetic Cigarette Smokers following switching to Combustion-Free Nicotine Delivery Systems: the DIASMOKE protocol
AUTHORS	Krysinski, Arkadiusz; Russo, Cristina; John, Sarah; Belsey, Jonathan; Campagna, Davide; Caponnetto, Pasquale; Vudu, Lorina; Lim, Chong; Purrello, Francesco; Di Mauro, Maurizio; Iqbal, Farrukh; Fluck, David; Franek, Edward; Polosa, Riccardo; Sharma, Pankaj

VERSION 1 – REVIEW

REVIEWER	Ann Verhaegen Antwerp University Hospital, Belgium
REVIEW RETURNED	03-Dec-2020

GENERAL COMMENTS	<p>This study can provide important data to the knowledge about the effect of non combustible smoking and their health effects in real life practice.</p> <p>I have some additional comments regarding the inclusion criteria. Is there a rationale for the BMI restriction? I suspect that body weight exceeding should be interpreted as, excess body weight of > 50 kg?</p> <p>Isn't giving initials and full birth date not a problem for privacy? month and year of birth and initials seem better.</p> <p>In the methods, the exact method of measurements should be mentioned (surely in the final paper) e.g. how is body composition measured?</p> <p>Wouldn't it be appropriate to include CRP or hsCRP in the measurements since that could give an indication of inflammation.</p>
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REVIEWER	Taeyun Kim The Armed Forces Goyang Hospital, Republic of Korea
REVIEW RETURNED	05-Jan-2021

GENERAL COMMENTS	<p>I have reviewed the study protocol entitled "International Randomized Controlled Trial evaluating metabolic syndrome in type 2 Diabetic Cigarette Smokers following switching to Combustion-Free Nicotine Delivery Systems: the DIASMOKE protocol". The protocol is dealing with a problem that is very actual. The study was well conducted by the authors. The method is clear and simple, and the statistical analyses are rigorous and are used properly. The results are very anticipated. However, I would like to recommend</p>
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	<p>defining inclusion criteria more precisely. For example, the authors selected BMI between 17.6 ~ 32.0 as an inclusion criteria. Cut-off values of nutritional status of European from WHO for underweight, normal, pre-obesity, and obesity are below 18.5, 18.5-24.9 , 25.0-29.9, and 30.0, respectively. Therefore, it would be better and seems more scientific if the selection criteria were based on scientific evidences.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Dr. Ann Verhaegen, University of Antwerp

Comments to the Author:

This study can provide important data to the knowledge about the effect of non combustible smoking and their health effects in real life practice.

Thank you for this positive statement.

I have some additional comments regarding the inclusion criteria. Is there a rationale for the BMI restriction?

A decision to introduce BMI as one of the inclusion criteria was based on the desire to exclude patients who are underweight or have a significant obesity in order to avoid extreme variability in the assessment of the primary endpoint of the study what could affect a statistical analysis. Please note that we have amended a typo, now correcting BMI values specified in the inclusion/exclusion criteria; this now has been changed on the basis of the official WHO recommendations for BMI between 18.5 and 34.9. We believe that includes a broad spectrum of patients and in the same time eliminates extreme BMI values that can introduce metabolic confounders.

I suspect that body weight exceeding should be interpreted as, excess body weight of > 50 kg?

Thank you for spotting this typo, which has been amended in the text.

Isn't giving initials and full birth date not a problem for privacy? month and year of birth and initials seem better.

We strongly agree that inputing the month and the year of birth instead of full birth date may help to protect patients' personal data. Adequate amendments have been introduced to the protocol as data safety is one of our main priorities.

In the methods, the exact method of measurements should be mentioned (surely in the final paper) e.g. how is body composition measured?

Thank you for highlighting this missing detail. Body weight and body composition outcomes will be measured using Tanita SC-240MA (Software Tanita Pro, Health Monitor Administrator, Version 3.4.0), a digital high-end scale and body composition monitor. Body weight and body composition

measurements will be carried out according to manufacturer's instructions. Each clinical site will be equipped with the same equipment. In addition, Tanita generated data will be counter checked against a recently validated formula to calculate body composition:

Han TS, Al-Gindan YY, Govan L, Hankey CR, Lean ME. Associations of BMI, waist circumference, body fat, and skeletal muscle with type 2 diabetes in adults. Acta diabetologica. 2019 Aug 1;56(8):947-54.

Please note that a detailed description of all DIASMOKE study assessments could not be included without exceeding the Journal's allotted word limits.

Wouldn't it be appropriate to include CRP or hsCRP in the measurements since that could give an indication of inflammation.

We do agree that including CRP/hsCRP as the inflammation indicators in the measurements section could provide additional insights on pathology processes and risk level. However, this additional information is ancillary compared to the far more robust primary endpoint of the study. Moreover, given the study is not powered for these assessment, CRP/hsCRP could be included only as an exploratory parameter. In that role, CRP can be added to the measurements.

Reviewer: 2

Dr. Taeyun Kim, The Armed Forces Goyang Hospital

Comments to the Author:

I have reviewed the study protocol entitled "International Randomized Controlled Trial evaluating metabolic syndrome in type 2 Diabetic Cigarette Smokers following switching to Combustion-Free Nicotine Delivery Systems: the DIASMOKE protocol". The protocol is dealing with a problem that is very actual. The study was well conducted by the authors. The method is clear and simple, and the statistical analyses are rigorous and are used properly. The results are very anticipated. However, I would like to recommend defining inclusion criteria more precisely. For example, the authors selected BMI between 17.6 ~ 32.0 as an inclusion criteria. Cut-off values of nutritional status of European from WHO for underweight, normal, pre-obesity, and obesity are below 18.5, 18.5-24.9, 25.0-29.9, and 30.0, respectively. Therefore, it would be better and seems more scientific if the selection criteria were based on scientific evidences.

Thank you for highlighting this point. Please note that we have amended this typo, now correcting BMI values specified in the inclusion/exclusion criteria; this now has been changed on the basis of the official WHO recommendations for BMI between 18.5 and 34.9. This is obviously based on scientific evidences.