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APPENDIX A6.1.4.12 HbA1C (GLYCATED HEMOGLOBIN) HEALTH EFFECTS OF SMOKING CESSATION

Short Term Health Effects

HbA1c (Glycated hemoglobin)

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1 BACKGROUND

The glycated hemoglobin HbA1c (more correctly written as HbA_{1c}) is a modified hemoglobin A, which is formed by non-enzymatic reaction of glucose (after rearrangement to its reactive aldehyde form) with hemoglobin. Since the percentage of HbA1c to total hemoglobin is proportional to the time-integrated glucose concentration in blood and the life-time of erythrocytes (in humans about 120 days), HbA1c is a long-term marker of blood glucose levels, reflecting the average glucose plasma concentrations over approximately 2 months prior to the test, with a range of 1 – 3 months [1]. These properties make HbA1c a 'gold standard' for the diagnosis, therapeutic monitoring and prognosis of patients with diabetes mellitus (DM).

Over the last three decades analytical methodology for the determination of HbA1c levels in humans as well as their interpretation has been markedly improved by appropriate standardization so that the application of HbA1c as a routine biomarker for diagnosis, prognosis and therapy monitoring in patients with assumed or proven DM (Type 1 and 2) can be regarded as well established [2-4].

A commonly accepted cut-off level of HbA1c between healthy subjects and patients with DM is 6.5 % [5, 6] , mainly based on the occurrence of retinopathy as a disease marker for DM [5]. However, lower cut-off levels of HbA1c (5.5 %) have also been suggested to be more optimal for predicting clinical endpoints in the population [7]. According to the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC), HbA1c is defined as HbA0 irreversibly glycated at the N-terminal valine of the b-chain and should be presentedin the unit mmol/mol. The cut-off level of 6.5 % corresponds with HbA1c adduct level of 48 mmol/mol (corresponding to a blood glucose level of 130 mg/dl). In this document most values for HbA1c are given in % rather than in mmol/mol, since this is still the most frequently used unit for this biomarker.

Age, sex, smoking status as well as red cell turnover are established influencing factors for HbA1c in healthy, non-diabetic people [8, 9].

The overwhelming number of studies of HbA1c in subjects have been conducted with DM patients or subjects at risk of developing DM. However, a number of nondiabetic predictors (including smoking and genetic factors) have also been identified as predictors for HbA1c [10]. Since smoking is known to negatively influence glucose metabolism both in healthy subjects and patients with DM [11, 12], there is the possibility of interactions of smoking and DM with implications on the HbA1c levels in subjects. The purpose of this document is to present and evaluate published information showing evidence for an association between smoking and HbA1c levels and provide an answer to the question: whether HbA1c is a suitable biomarker of effect for assessing modified risk tobacco products (MRTPs).

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2 METHODS

The published information for generating the present document was collected from the following sources:

(1) Monographs on biomarkers of effect and smoking:

- US Surgeon General Report 2010 [13]
- Life Sciences Research Office (LSRO) Report of 2007 [14]

(2) Search 1 in the PubMed literature data base on 08.04.2015 for reviews on HbA1c; search string: “HbA1c[Title], Filters: Review”

(3) Search 2 in the PubMed literature data base on 08.04.2015 for smoking-related studies on HbA1c, limited to the time period 2008 to present and articles in English; search string: “(((((((((HbA1c[Title/Abstract]) AND ("2008"[Date - Publication] : "3000"[Date - Publication]))) AND English[Language])) AND (smokers[Title] OR smoking[Title] OR nicotine replacement[Title] OR cessation[Title])))))) OR (((((((HbA1c[Title]) AND ("2008"[Date - Publication] : "3000"[Date - Publication]))) AND English[Language])) AND (smokers[Title/Abstract] OR smoking[Title/Abstract] OR nicotine replacement[Title/Abstract] OR cessation[Title/Abstract])))))”

(4) Search 3 in the PubMed literature data base on 08.04.2015 for the association between HbA1c and cardiovascular disease, limited to the time period 2008 to present and articles in English; search string: “(((((((HbA1c[Title]) AND ("2008"[Date - Publication] : "3000"[Date - Publication]))) AND English[Language])) AND (cardiovascular disease[Title/Abstract])))”

(5) Search 4 in PubMed literature data base on 08.04.2015 for the association between HbA1c and respiratory diseases_limited to the time period 2008 to present and articles in English; search string: “(((((((HbA1c[Title/Abstract]) AND ("2008"[Date - Publication] : "3000"[Date - Publication]))) AND English[Language])) AND (respiratory disease[Title/Abstract])))”

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(6) Search 5 in PubMed literature data base on 08.04.2015 for the association between HbA1c and respiratory diseases limited to the time period 2008 to present and articles in English; search string: "(((((((((HbA1c[Title]) AND ("2008"[Date - Publication] : "3000"[Date - Publication]))) AND English[Language])) AND (cancer[Title/Abstract])))))"

(7) Additionally, cited references of apparent relevance from articles retrieved as described above were used for generating this dossier.

Studies were selected for evaluations in Chapter 4 ('Biomarker-disease link') and Chapter 5 ('Smoking-biomarker link') according to the following inclusion criteria:

A: Association between HbA1c and cardiovascular diseases (CVD) in a human cohort was investigated

B: Association between HbA1c and respiratory diseases in a human cohort was investigated

C: Association between HbA1c and any other disease in a human cohort was investigated

D: Differences between in HbA1c levels between smokers and non-smokers were studied

E: The dose-response relationship between smoking intensity (determined for example by daily cigarette consumption, pack-year or cotinine levels) and HbA1c level was studied

F: The effect of smoking cessation on the HbA1c level was studied

G: The effect of switching from conventional cigarettes to a modified risk tobacco product (MRTP) or a nicotine products on the HbA1c level was studied

R: Review article on HbA1c

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Reviews were used for generating Chapter 1 ('Background') and, if suitable, also for Chapters 4 and 5.

Studies not fulfilling any of the inclusion criteria A – G and R were excluded from the evaluation (assigned as 0x, x (reason for exclusion) = 1 to 5).

01 No usable data or information on HbA1c were presented

02 Clinical study with patients, focus on diagnosis, therapy and prognosis

03 Population investigated is not relevant for the purpose of this document (e.g. children, pregnant women, ill persons)

04 The topic investigated is not relevant for smoking or a smoking-related disease

05 Animal or *in vitro* studies with no obvious relation to humans.

3 FINDINGS

From Source 1, 4 articles [12, 15-17] were extracted (all originating from the Surgeon General Report 2010 [13]). The LSRO monograph [14] did not mention HbA1c as a biomarker of effect for smoking.

The distribution of articles according to the sources 1 – 7 described in Chapter 2 ('Methods') and according the inclusion criteria A – G and R are summarized in Table 1. The individual articles according to sources and assignment to inclusion criteria are compiled in Appendix 1.

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Table 1. Search results and distribution across the inclusion criteria.

Source (Description)	All	Relevant	Inclusion criteria[a]								Ex-cluded
			A	B	C	D	E	F	G	R	
1 (Monographs)	4	4	3	-	-	1	-	-	-	1	0
2 (Search 1, reviews)	79	45	8	-	5	-	-	-	-	45	34
3 (Search 2, smoking)	52	36	15	-	16	20	2	2	-	1	16
4 (Search 3, CVD)	29	21	19	-	10	2	-	-	-	1	8
5 (Search 4, resp. dis.)	4	1	-	-	-	-	-	-	-	1	3
6 (Search 5, cancer)	12	9	2	-	8	-	-	-	-	-	3
7 (Cited articles)	35	30	2	-	2	26	2	5	-	-	3
Sum	215[b]	146	49	0	41	49	4	7	0	49	67

[a] Note that an article could fulfil several inclusion criteria

[b] Deviation from the 203 articles listed in Appendix 1 is caused by some overlap between the search results yielding identical articles

Of the 215 articles retrieved from the various sources, 146 appeared to be relevant to be considered for the generation of this document, 67 publications were of no or very limited relevance for this purpose. Most articles retrieved deal with the criteria CVD (A, N = 49), other diseases, in particular cancer (C, N = 41) and smoking (D, N=49) or were reviews. No separate search for the association of HbA1c with other diseases was performed, since the category 'other diseases' was already well represented in Searches 1 - 5. There were 49 articles which considered the relationship between HbA1c and smoking. The aspect of smoking cessation (F) was dealt with in 7 studies, whereas the dose-relationship between smoking and HbA1c levels was considered in 4 articles. No relevant studies were found which look at the association between HbA1c and respiratory diseases (B) or change of HbA1c level after switching to an MRTP (G).

It should be noted that the classification of the retrieved articles was done after a first inspection (usually by reading the abstract). The final classification can deviate from this assignment. However, the distribution of the articles according to the defined criteria was

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very similar to that shown in Table 1, thus reflecting the knowledge and the weight of evidence available for the various categories.

4 BIOMARKER-DISEASE LINK

Since DM is a major risk factor for CVD and other diseases, HbA1c, one of the most important disease markers for DM, is inevitably associated with the DM-related diseases. It is, therefore, important to evaluate the evidence for HbA1c as an independent risk factor for disease and mortality. The most suitable information for this purpose could be derived from studies which investigated the association between HbA1c and disease or mortality in non-diabetic persons. However, only a few studies of this type have been performed. By far the largest number of studies on the associations between HbA1c and diseases were conducted with DM patients of both type 1 (T1DM) and type 2 (T2DM) diabetes. Another difficulty is the fact that diagnosis of DM in many cases is not unequivocal. Depending on the cut-off level of, for example, HbA1c, a subject could be classified as diabetic, pre-diabetic or healthy. This has to be considered when associations between HbA1c and diseases or mortality are evaluated.

4.1 Cardiovascular disease

In epidemiological studies of Gao et al. [18] (people older than 69 years), Gerstein [19] (non-diabetic patients with heart failure), van 'Riet et al. [20] (particularly women without DM) and Hernandez et al. [7] (subjects without DM) with non-diabetic subjects, significant associations between HbA1c and CVD, CV death or total mortality were observed. On the other hand, Egg-Olofsson et al. [21] in an observational study showed progressively increasing risks of coronary heart disease (CHD), CVD and total mortality with higher HbA1c (>6.5 %), and no risk increase at low HbA1c levels (< 6.5 %). Chamnan et al. [22] reported that addition of information on change in HbA1c over 3 years did not improve the prediction of CVD over and above information on HbA1c and other major cardiovascular risk factors from a single time point in a non-diabetic population.

In a series of other studies with T1DM or T2DM patients, significant associations between HbA1c and various CVDs were reported [23-28]. Risk for CVD and related diseases in DM patients per 1 % of HbA1c increase was usually twice as high as compared to non-diabetic subjects. In the latter group, the magnitude of this risk increased by approximately 10-20% per 1% increase in HbA1c levels [29].

Variability (fluctuation) of HbA1c (as a result of poor glycemic control), rather than the increase in HbA1c level, appears to increase the risk for disease. Takao et al. [23] reported that HbA1c variability is a predictor of all-cause mortality, especially non-cancer mortality including CVD, in patients with T2DM, independent of mean HbA1c level. In contrast, mean HbA1c, but not HbA1c variability, might predict cancer mortality (see Chapter 4.3). Luk et al. (2013) [30] found that long-term glycemic variability expressed by SD of HbA1c predicted development of renal and cardiovascular complications in T2DM patients. Bouchi et al. [31] suggested that variability of HbA1c may be a predictor of incident CVD in Japanese patients with T2DM.

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4.2 Respiratory disease

Almost no evidence for an association between HbA1c and respiratory diseases was found.

Lecube et al. [32] reported that fasting glucose and HbA1c independently predicted FEV1 (forced expiratory volume in 1 s, negatively correlated) and RV (residual volume, positively correlated) in morbidly obese women.

It is well established that DM is associated with an increased all-cause mortality (including respiratory diseases) and also cancer risk [1, 33, 34].

In apparently healthy people, a significant association between HbA1c and all-cause mortality [18, 20, 35, 36] and various cancer risks [34, 35] has also been reported. There are many more additional studies which found a significantly positive association between HbA1c and total mortality [21, 23, 25, 27, 33] and cancer risk [23, 37-39] in patients with T1DM or T2DM. In one study [1], no association between HbA1c and cancer risk was reported.

It has been reported that the aggressiveness of tumors in DM patients was higher in subjects with higher HbA1c levels [37, 38].

There are several reports that chronic kidney diseases [30, 40, 41] and periodontitis [1, 42, 43] in diabetic patients were significantly associated with HbA1c. Furthermore, diabetic patients with higher HbA1c levels were found to be more likely to suffer from depression [44, 45].

5 SMOKING-BIOMARKER LINK

Most studies on an association between smoking and HbA1c were performed in populations of diabetic patients. It is self-evident that for the evaluation of HbA1c as a biomarker of effect for smoking, studies with healthy (nondiabetic) subjects would be more suitable.

Recently, Soulimane et al. [46] performed a meta-analysis for HbA1c levels in current, ex- and never-smokers including 14 studies with predominantly T2DM populations. As a summary result from their meta-analysis, the authors reported that HbA1c was 0.10% (95% CI: 0.08-0.12%) higher in current smokers and 0.03% (0.01-0.05) higher in ex-smokers, compared with never-smokers. The difference between current-smokers and never-smokers was significantly greater in men 0.13 (0.11-0.15) % than in women 0.05 (0.02-0.07) %. Male ex-smokers had higher HbA1c levels than never-smokers while female ex-smokers had lower HbA1c values. From their meta-analysis, the authors concluded that HbA1c was higher in smokers than in non-smokers, whereas the opposite was observed for fasting plasma glucose (FPG) and plasma glucose after 2h (2H-PG) in glucose tolerance tests.

Soulimane et al. [46] also discussed possible mechanisms by which smoking might lead to the observed significantly elevated HbA1c levels compared to non-smokers. Apart from mechanisms by which smoking might increase the risk for DM [47, 48], it is also possible that smoking can directly interfere with the glycation of hemoglobin to yield

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HbA1c, for example by increasing the permeability of the erythrocyte membrane or by interference with the analytical determination of HbA1c [8]. Smith et al. [49] reported increased HbA1c levels in vitro under decreased oxygen tension and increased 2,3-diphosphoglycerate conditions, both factors known to be influenced by smoking.

Table 2 summarizes results for HbA1c levels in smokers, non-smokers and ex-smokers form various populations.

In many, but not all, studies [50-52] significantly higher HbA1c levels in smokers compared to non-smokers were observed. Absolute differences in HbA1c levels between smokers and non-smokers are most frequently (particularly in the very large studies reviewed by Soulimane et al. [46]) in the range of 0.1-0.5 %, irrespective of the DM status. Differences between smokers and non-smokers are usually higher in diabetic compared to nondiabetic populations. The relative difference in the HbA1c levels, therefore, is well below 10 %. Although the inter- and intra-individual variation in HbA1c is low, the small difference between smokers and non-smokers would require large subject numbers to show significant effects in the HbA1c level after stopping smoking (see Section 5.2) or as a result of switching to MRTPs.

Table 2. Results for HbA1c levels in smokers, non-smokers and ex-smokers form various populations.

Author (reference)	Population	Smokers (S)	Non-smokers (NS)	p-Values and remarks
Simon et al. [53]	Nondiabetic adults from a French working population	Mean±SD, %: Male S (N=570): 5.11±0.51 Female S (N=403): 5.09±0.54	Mean±SD, %: Male NS (N=991): 4.99±0.54 Female NS (N=1276): 5.06±0.56	Males and females: P<0.001
Nilsson et al. [54]	140 Hypertensive and 51 normo-tensive subjects from Sweden	Mean±SD, %: S (N=41): 4.86±0.54	Mean±SD, %: NS (N=150): 4.67±0.55	P=0.048 Differences between S and NS were similar in hyper- and normotensive subjects

(table continues)

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Author (reference)	Population	Smokers (S)	Non-smokers (NS)	p-Values and remarks
Targher et al. [55]	Non-insulin-dependent patients with DM	Mean±SE, %: S (N=28): 6.7±0.2	Mean±SE, %: NS (N=12): 6.1±1.2	Not significant
Boeing et al. [51]	Middle-aged, nondiabetic population in Germany	Mean±SE, %: Male S (N=214): 5.07±0.05 Female S (N=201): 4.76±0.05	Mean±SE, %: Male NS (N=228): 4.89±0.04 Male Ex-S (N=302): 4.89±0.05 Female NS (N=201): 4.76±0.05 Female Ex-S (N=224): 4.59±0.05	No significant differences between S and NS
Gulliford et al. [56]	Nondiabetic subjects ≥16 years from England	Random effect model, coefficients for HbA1c (%): Never S (N=4376): - S (N=660; 1-9 cig/d): 0.125 S (N=1108; 10-19 cig/d): 0.189 S (N=911; 20+ cig/d): 0.277 Ex-S (N=2695): 0.017		P<0.001 Physical activity and alcohol were negatively associated
Baggio et al. [48]	Patients with T2DM and abnormal albumin excretion	Mean±SD, %: S (N=48): 8.6±1.6	Mean±SD, %: S (N=48): 7.6±1.5	P=0.002
Nilsson et al. [57]	Diabetic patients (T1DM and T2DM) from Sweden	Mean±SD, %: S (N=1622): 7.67±0.41	Mean±SD, %: NS (N=9718): 7.21±1.34	P<0.001 Regression model: Smoking was independently associated with HbA1c

(table continues)

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Author (reference)	Population	Smokers (S)	Non-smokers (NS)	p-Values and remarks
Anan et al. [50]	Japanese patients with T2DM	Mean±SD, %: S (N=22): 7.8±1.3	Mean±SD, %: NS (N=30): 7.7±1.1	Not significant
Schwab et al. [58]	Children and adolescents (11-17 years) with Type 1 diabetes	Median (68.5 % CI)[a], ng/mL: All exposed subjects (active and passive, N=19): 9.3 (9.0-10.9) Age-matched active S (N=12): 9.3 (8.9-10.9)	Median (68.5 % CI)[b], ng/mL: Unexposed subjects (N=73): 7.4 (7.3-7.5) Age-matched never S (N=12): 8.2 (7.3-8.8)	P<0.001 Smoking (not clear which parameter) correlated with HbA1c levels: r=0.396, P=0.0002)

5.1 Smoking

Only sparse information is available on the dose-response relationship between HbA1c and the smoking dose, determined for example by daily cigarette consumption (CPD), pack-years or suitable biomarkers of exposure such as cotinine in body fluids. As shown for some studies in Table 2, a significant increase with the smoking dose assessed by CPD, pack-years or plasma cotinine concentrations was reported by Gulliford et al. [56], Schwab et al. [58], Clair et al. [59], Vlassopoulos et al. [60] and Ohkuma et al. [61]. Although the associations between smoking intensity and HbA1c were found to be only low to moderate, the available evidence on the dose-response relationship would qualify HbA1c as a suitable biomarker of effect.

5.2 Smoking cessation

Since the half-life of HbA1c is determined by the lifespan of red blood cells (~ 4 months), it is obvious that changes in the HbA1c levels can only be expected in long-term observations (months to years). In a number of studies [11, 56, 59-63] (partly summarized in Table 2), HbA1c in ex-smokers in addition to current and never-smokers was determined. There is general agreement in the results that HbA1c levels in ex-smokers are close to those of never-smokers. Hokanson et al. [64] found that in T2DM patients who quit smoking for 3 months (the shortest time period of quitting reported in the literature for HbA1c) experienced a reduction in HbA1c from 8.9 to <7.0 %.

The HbA1c data available for ex-smokers and smoking cessation studies would generally qualify HbA1c as a suitable long-term (months to years) biomarker of effect. However, the size of the change in HbA1c levels presents a severe limitation.

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6 CONCLUSION

The role of HbA1c as a disease marker for DM with good to excellent properties in the diagnosis, prognosis and therapeutic control of this widespread disease is well established. There is strong evidence that smoking leads to a dose-dependent increase in HbA1c, both in nondiabetic and diabetic populations. This observation is in concordance with frequently reported findings that smoking is a risk factor for T2DM. Smoking cessation for months to years leads to a decrease in HbA1c levels, achieving almost never-smoker levels. However, the smoking-related effects on HbA1c are relatively small (< 10 % in relative units). Furthermore, it is not yet clear whether smoking affects the HbA1c level by perturbing the glucose homeostasis or by a 'secondary' mechanism.

The strength of the evidence for the suitability of HbA1c as a biomarker of effect is summarized in Table 3.

Taken together, the information available does not provide strong evidence for the suitability of HbA1c as a biomarker of effect for the assessment of MRTPs. However, HbA1c should be considered as long-term biomarker in larger populations who have switched to MRTPs (e.g. in post-market studies).

6.1 Role in MRTP assessment

Table 3. Strength of evidence for MRTP assessment.

Property	Evidence
Biological plausibility	HbA1c is a proven biomarker for the integral blood glucose level, covering a time period of about 2 months. This property makes HbA1c an established marker for diagnosis, prognosis and therapeutic control of DM.
Dose-response	Differences between smokers and non-smokers (zero dose) were reported for diabetic and non-diabetic subjects in many studies (Table 2). Observed increases in smokers compared to non-smokers are usually low (< 10 % in relative units). There is also some evidence that HbA1c increases with the smoking dose as determined by daily cigarette consumption, pack-years or cotinine levels in plasma.
Benchmark to cessation	Long-term (months to years) quitting of smoking leads to a reduction in HbA1c levels, achieving almost never-smoker levels. Most of this evidence comes from data obtained with former smokers.

(table continues)

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Property	Evidence
Consistency[a]	Available data for HbA1c and smoking are mostly, but not completely, consistent.
Coherence[b]	Epidemiological, animal and *in vitro* data proving the role of HbA1c as an indicator of long-term blood glucose levels and its control are coherent. The role of smoking as an elevator of HbA1c has not yet been fully investigated with various approaches so that coherence cannot be finally judged.

[a] Consistent findings in various studies strengthens the likelihood that the finding is true

[b] Coherence of findings from epidemiological, laboratory, animal and *in vitro* studies increases the likelihood that the result is true

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6.2 References used in the text

1. Miao Jonasson J, Cederholm J, Eliasson B, Zethelius B, Eeg-Olofsson K, Gudbjornsdottir S. HbA1C and cancer risk in patients with type 2 diabetes--a nationwide population-based prospective cohort study in Sweden. PLoS ONE. 2012;7(6):e38784. doi: 10.1371/journal.pone.0038784. Epub 2012 Jun 14.

2. Juarez DT, Demaris KM, Goo R, Mnatzaganian CL, Wong Smith H. Significance of HbA1c and its measurement in the diagnosis of diabetes mellitus: US experience. Diabetes Metab Syndr Obes. 2014;7:487-94.(doi):10.2147/DMSO.S39092. eCollection 2014.

3. Weykamp C. HbA1c: a review of analytical and clinical aspects. Ann Lab Med. 2013;33(6):393-400. doi: 10.3343/alm.2013.33.6.393. Epub Oct 17.

4. Little RR, Rohlfing CL. The long and winding road to optimal HbA1c measurement. Clin Chim Acta. 2013;418:63-71.(doi):10.1016/j.cca.2012.12.026. Epub 3 Jan 11.

5. Kowall B, Rathmann W. HbA1c for diagnosis of type 2 diabetes. Is there an optimal cut point to assess high risk of diabetes complications, and how well does the 6.5% cutoff perform? Diabetes Metab Syndr Obes. 2013;6:477-91.(doi):10.2147/DMSO.S39093.

6. Benhalima K, Standl E, Mathieu C. The importance of glycemic control: how low should we go with HbA1c? Start early, go safe, go low. J Diabetes Complications. 2011;25(3):202-7. doi: 10.1016/j.jdiacomp.2010.03.002. Epub May 11.

7. Hernandez D, Espejo-Gil A, Bernal-Lopez MR, Mancera-Romero J, Baca-Osorio AJ, Tinahones FJ, et al. Association of HbA1c and cardiovascular and renal disease in an adult Mediterranean population. BMC Nephrol. 2013;14:151.(doi):10.1186/471-2369-14-151.

8. Higgins T, Cembrowski G, Tran D, Lim E, Chan J. Influence of variables on hemoglobin A1c values and nonheterogeneity of hemoglobin A1c reference ranges. J Diabetes Sci Technol. 2009;3(4):644-8.

9. Pani LN, Korenda L, Meigs JB, Driver C, Chamany S, Fox CS, et al. Effect of aging on A1C levels in individuals without diabetes: evidence from the Framingham Offspring Study and the National Health and Nutrition Examination Survey 2001-2004. Diabetes Care. 2008;31(10):1991-6. doi: 10.2337/dc08-0577. Epub 2008 Jul 15.

10. Jansen H, Stolk RP, Nolte IM, Kema IP, Wolffenbuttel BH, Snieder H. Determinants of HbA1c in nondiabetic Dutch adults: genetic loci and clinical and lifestyle parameters, and their interactions in the Lifelines Cohort Study. J Intern Med. 2013;273(3):283-93. doi: 10.1111/joim.12010. Epub 2012 Dec 5.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

11. Gerber PA, Locher R, Schmid B, Spinas GA, Lehmann R. Smoking is associated with impaired long-term glucose metabolism in patients with type 1 diabetes mellitus. Nutr Metab Cardiovasc Dis. 2013;23(2):102-8. doi: 10.1016/j.numecd.2011.08.007. Epub Nov 25.

12. Eliasson B. Cigarette smoking and diabetes. Prog Cardiovasc Dis. 2003;45(5):405-13.

13. U.S. Department of Health and Human Services. How tobacco smoke causes disease: the biology and behavioral basis for smoking-attributable disease: a report of the Surgeon General. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health. 2010.

14. Life Sciences Research Office (LSRO). Biological effects assessment in the evaluation of potential reduced-risk tobacco products. Brownawell AM, editor. Bethesda, Maryland, USA2007.

15. Bott U, Jorgens V, Grusser M, Bender R, Muhlhauser I, Berger M. Predictors of glycaemic control in type 1 diabetic patients after participation in an intensified treatment and teaching programme. Diabet Med. 1994;11(4):362-71.

16. Lundman BM, Asplund K, Norberg A. Smoking and metabolic control in patients with insulin-dependent diabetes mellitus. J Intern Med. 1990;227(2):101-6.

17. Sargeant LA, Khaw KT, Bingham S, Day NE, Luben RN, Oakes S, et al. Cigarette smoking and glycaemia: the EPIC-Norfolk Study. European Prospective Investigation into Cancer. Int J Epidemiol. 2001;30(3):547-54.

18. Gao L, Matthews FE, Sargeant LA, Brayne C. An investigation of the population impact of variation in HbA1c levels in older people in England and Wales: from a population based multi-centre longitudinal study. BMC Public Health. 2008;8:54.(doi):10.1186/471-2458-8-54.

19. Gerstein HC, Swedberg K, Carlsson J, McMurray JJ, Michelson EL, Olofsson B, et al. The hemoglobin A1c level as a progressive risk factor for cardiovascular death, hospitalization for heart failure, or death in patients with chronic heart failure: an analysis of the Candesartan in Heart failure: Assessment of Reduction in Mortality and Morbidity (CHARM) program. Arch Intern Med. 2008;168(15):1699-704. doi: 10.001/archinte.168.15..

20. van 't Riet E, Rijkelijkhuizen JM, Alssema M, Nijpels G, Stehouwer CD, Heine RJ, et al. HbA1c is an independent predictor of non-fatal cardiovascular disease in a Caucasian population without diabetes: a 10-year follow-up of the Hoorn Study. Eur J Prev Cardiol. 2012;19(1):23-31. doi: 10.1097/HJR.0b013e32833b0932. Epub 2011 Jan 28.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

21. Eeg-Olofsson K, Cederholm J, Nilsson PM, Zethelius B, Svensson AM, Gudbjornsdottir S, et al. New aspects of HbA1c as a risk factor for cardiovascular diseases in type 2 diabetes: an observational study from the Swedish National Diabetes Register (NDR). J Intern Med. 2010;268(5):471-82. doi: 10.1111/j.365-2796.010.02265.x.

22. Chamnan P, Simmons RK, Khaw KT, Wareham NJ, Griffin SJ. Change in HbA1c over 3 years does not improve the prediction of cardiovascular disease over and above HbA1c measured at a single time point. Diabetologia. 2013;56(5):1004-11. doi: 10.7/s00125-013-2854-8. Epub 2013 Feb 12.

23. Takao T, Matsuyama Y, Yanagisawa H, Kikuchi M, Kawazu S. Association between HbA1c variability and mortality in patients with type 2 diabetes. J Diabetes Complications. 2014;28(4):494-9. doi: 10.1016/j.jdiacomp.2014.02.006. Epub Feb 18.

24. Kilpatrick ES, Rigby AS, Atkin SL. Mean blood glucose compared with HbA1c in the prediction of cardiovascular disease in patients with type 1 diabetes. Diabetologia. 2008;51(2):365-71. Epub 2007 Nov 27.

25. Andersson C, van Gaal L, Caterson ID, Weeke P, James WP, Coutinho W, et al. Relationship between HbA1c levels and risk of cardiovascular adverse outcomes and all-cause mortality in overweight and obese cardiovascular high-risk women and men with type 2 diabetes. Diabetologia. 2012;55(9):2348-55. doi: 10.1007/s00125-012-2584-3. Epub 2012 May 26.

26. Nathan DM, McGee P, Steffes MW, Lachin JM. Relationship of glycated albumin to blood glucose and HbA1c values and to retinopathy, nephropathy, and cardiovascular outcomes in the DCCT/EDIC study. Diabetes. 2014;63(1):282-90. doi: 10.2337/db13-0782. Epub 2013 Aug 29.

27. Xu L, Chan WM, Hui YF, Lam TH. Association between HbA1c and cardiovascular disease mortality in older Hong Kong Chinese with diabetes. Diabet Med. 2012;29(3):393-8. doi: 10.1111/j.464-5491.2011.03456.x.

28. Pacilli A, De Cosmo S, Trischitta V, Bacci S. Role of relationship between HbA1c, fibrinogen and HDL-cholesterol on cardiovascular disease in patients with type 2 diabetes mellitus. Atherosclerosis. 2013;228(1):247-8. doi: 10.1016/j.atherosclerosis.2013.02.010. Epub Feb 20.

29. Khaw KT. Elevated HbA1c level: a risk factor for cardiovascular disease mortality in patients with chronic heart failure? Nat Clin Pract Endocrinol Metab. 2009;5(3):130-1. doi: 10.1038/ncpendmet69.

30. Luk AO, Ma RC, Lau ES, Yang X, Lau WW, Yu LW, et al. Risk association of HbA1c variability with chronic kidney disease and cardiovascular disease in type 2 diabetes: prospective analysis of the Hong Kong Diabetes Registry. Diabetes Metab Res Rev. 2013;29(5):384-90. doi: 10.1002/dmrr.2404.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

31. Bouchi R, Babazono T, Mugishima M, Yoshida N, Nyumura I, Toya K, et al. Fluctuations in HbA1c are associated with a higher incidence of cardiovascular disease in Japanese patients with type 2 diabetes. J Diabetes Investig. 2012;3(2):148-55. doi: 10.1111/j.2040-1124.2011.00155.x.

32. Lecube A, Sampol G, Munoz X, Hernandez C, Mesa J, Simo R. Type 2 diabetes impairs pulmonary function in morbidly obese women: a case-control study. Diabetologia. 2010;53(6):1210-6. doi: 10.007/s00125-010-1700-5. Epub 2010 Mar 9.

33. Sluik D, Boeing H, Montonen J, Kaaks R, Lukanova A, Sandbaek A, et al. HbA1c measured in stored erythrocytes is positively linearly associated with mortality in individuals with diabetes mellitus. PLoS ONE. 2012;7(6):e38877. doi: 10.1371/journal.pone.0038877. Epub 2012 Jun 13.

34. de Beer JC, Liebenberg L. Does cancer risk increase with HbA1c, independent of diabetes? Br J Cancer. 2014;110(9):2361-8. doi: 10.1038/bjc.2014.150. Epub Mar 27.

35. Levitan EB, Liu S, Stampfer MJ, Cook NR, Rexrode KM, Ridker PM, et al. HbA1c measured in stored erythrocytes and mortality rate among middle-aged and older women. Diabetologia. 2008;51(2):267-75. Epub 2007 Nov 28.

36. Brewer N, Wright CS, Travier N, Cunningham CW, Hornell J, Pearce N, et al. A New Zealand linkage study examining the associations between A1C concentration and mortality. Diabetes Care. 2008;31(6):1144-9. doi: 10.2337/dc07-74. Epub 008 Feb 25.

37. Siddiqui AA, Spechler SJ, Huerta S, Dredar S, Little BB, Cryer B. Elevated HbA1c is an independent predictor of aggressive clinical behavior in patients with colorectal cancer: a case-control study. Dig Dis Sci. 2008;53(9):2486-94. doi: 10.1007/s10620-008-0264-4. Epub 2008 Apr 12.

38. Hong SK, Lee ST, Kim SS, Min KE, Byun SS, Cho SY, et al. Significance of preoperative HbA1c level in patients with diabetes mellitus and clinically localized prostate cancer. Prostate. 2009;69(8):820-6. doi: 10.1002/pros.20932.

39. Fan Y, Huang XD, Zhang H, Wu J, Zhang XX, Luo HS. Association between serum HbA1c levels and adenomatous polyps in patients with the type 2 diabetes mellitus. Minerva Endocrinol. 2014;8:8.

40. Aggarwal J, Kumar M. Prevalence of microalbuminuria among rural North Indian Population with diabetes mellitus and its correlation with glycosylated haemoglobin and smoking. J Clin Diagn Res. 2014;8(7):CC11-3. doi: 0.7860/JCDR/2014/9758.4613. Epub 2014 Jul 20.

41. Wang C, Song J, Ma Z, Yang W, Li C, Zhang X, et al. Fluctuation between fasting and 2-H postload glucose state is associated with chronic kidney disease in previously diagnosed type 2 diabetes patients with HbA1c >/= 7%. PLoS One. 2014;9(7):e102941. doi: 10.1371/journal.pone.0102941. eCollection 2014.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

42. Hodge PJ, Robertson D, Paterson K, Smith GL, Creanor S, Sherriff A. Periodontitis in non-smoking type 1 diabetic adults: a cross-sectional study. J Clin Periodontol. 2012;39(1):20-9. doi: 10.1111/j.600-051X.2011.01791.x. Epub 2011 Oct 31.

43. Susanto H, Nesse W, Dijkstra PU, Hoedemaker E, van Reenen YH, Agustina D, et al. Periodontal inflamed surface area and C-reactive protein as predictors of HbA1c: a study in Indonesia. Clin Oral Investig. 2012;16(4):1237-42. doi: 10.007/s00784-011-0621-0. Epub 2011 Oct 20.

44. Melin EO, Thunander M, Landin-Olsson M, Hillman M, Thulesius HO. Depression, smoking, physical inactivity and season independently associated with midnight salivary cortisol in type 1 diabetes. BMC Endocr Disord. 2014;14:75.(doi):10.1186/472-6823-14-75.

45. Melin EO, Thunander M, Svensson R, Landin-Olsson M, Thulesius HO. Depression, obesity, and smoking were independently associated with inadequate glycemic control in patients with type 1 diabetes. Eur J Endocrinol. 2013;168(6):861-9. doi: 10.1530/EJE-13-0137. Print 2013 Jun.

46. Soulimane S, Simon D, Herman WH, Lange C, Lee CM, Colagiuri S, et al. HbA1c, fasting and 2 h plasma glucose in current, ex- and never-smokers: a meta-analysis. Diabetologia. 2014;57(1):30-9. doi: 10.1007/s00125-013-3058-y. Epub 2013 Sep 25.

47. Willi C, Bodenmann P, Ghali WA, Faris PD, Cornuz J. Active smoking and the risk of type 2 diabetes: a systematic review and meta-analysis. JAMA. 2007;298(22):2654-64.

48. Baggio B, Budakovic A, Dalla Vestra M, Saller A, Bruseghin M, Fioretto P. Effects of cigarette smoking on glomerular structure and function in type 2 diabetic patients. J Am Soc Nephrol. 2002;13(11):2730-6.

49. Smith RJ, Koenig RJ, Binnerts A, Soeldner JS, Aoki TT. Regulation of hemoglobin AIc formation in human erythrocytes in vitro. Effects of physiologic factors other than glucose. J Clin Invest. 1982;69(5):1164-8.

50. Anan F, Takahashi N, Shinohara T, Nakagawa M, Masaki T, Katsuragi I, et al. Smoking is associated with insulin resistance and cardiovascular autonomic dysfunction in type 2 diabetic patients. Eur J Clin Invest. 2006;36(7):459-65.

51. Boeing H, Weisgerber UM, Jeckel A, Rose HJ, Kroke A. Association between glycated hemoglobin and diet and other lifestyle factors in a nondiabetic population: cross-sectional evaluation of data from the Potsdam cohort of the European Prospective Investigation into Cancer and Nutrition Study. Am J Clin Nutr. 2000;71(5):1115-22.

52. Kotani K, Sakane N, Miyamoto M, Yamada K, Taniguchi N. Influence of smoking habits on the GA/HbA1c ratio in patients with type 1 diabetes mellitus. Med Princ Pract. 2010;19(5):415-7.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

53. Simon D, Senan C, Garnier P, Saint-Paul M, Papoz L. Epidemiological features of glycated haemoglobin A1c-distribution in a healthy population. The Telecom Study. Diabetologia. 1989;32(12):864-9.

54. Nilsson PM, Lind L, Pollare T, Berne C, Lithell HO. Increased level of hemoglobin A1c, but not impaired insulin sensitivity, found in hypertensive and normotensive smokers. Metabolism. 1995;44(5):557-61.

55. Targher G, Alberiche M, Zenere MB, Bonadonna RC, Muggeo M, Bonora E. Cigarette smoking and insulin resistance in patients with noninsulin-dependent diabetes mellitus. J Clin Endocrinol Metab. 1997;82(11):3619-24.

56. Gulliford MC, Ukoumunne OC. Determinants of glycated haemoglobin in the general population: associations with diet, alcohol and cigarette smoking. Eur J Clin Nutr. 2001;55(7):615-23.

57. Nilsson PM, Gudbjornsdottir S, Eliasson B, Cederholm J. Smoking is associated with increased HbA1c values and microalbuminuria in patients with diabetes--data from the National Diabetes Register in Sweden. Diabetes Metab. 2004;30(3):261-8.

58. Schwab KO, Doerfer J, Hallermann K, Krebs A, Schorb E, Krebs K, et al. Marked smoking-associated increase of cardiovascular risk in childhood type 1 diabetes. Int J Adolesc Med Health. 2008;20(3):285-92.

59. Clair C, Bitton A, Meigs JB, Rigotti NA. Relationships of cotinine and self-reported cigarette smoking with hemoglobin A1c in the U.S.: results from the National Health and Nutrition Examination Survey, 1999-2008. Diabetes Care. 2011;34(10):2250-5. doi: 10.337/dc11-0710. Epub 2011 Aug 11.

60. Vlassopoulos A, Lean ME, Combet E. Influence of smoking and diet on glycated haemoglobin and 'pre-diabetes' categorisation: a cross-sectional analysis. BMC Public Health. 2013;13:1013.(doi):10.1186/471-2458-13-1013.

61. Ohkuma T, Iwase M, Fujii H, Kaizu S, Ide H, Jodai T, et al. Dose- and time-dependent association of smoking and its cessation with glycemic control and insulin resistance in male patients with type 2 diabetes mellitus: the fukuoka diabetes registry. PLoS One. 2015;10(3):e0122023. doi: 10.1371/journal.pone.. eCollection 2015.

62. Choi YJ, Park JS, Kim U, Lee SH, Son JW, Shin DG, et al. Changes in smoking behavior and adherence to preventive guidelines among smokers after a heart attack. J Geriatr Cardiol. 2013;10(2):146-50. doi: 10.3969/j.issn.1671-5411.2013.02.006.

63. Voulgari C, Katsilambros N, Tentolouris N. Smoking cessation predicts amelioration of microalbuminuria in newly diagnosed type 2 diabetes mellitus: a 1-year prospective study. Metabolism. 2011;60(10):1456-64.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

64. Hokanson JM, Anderson RL, Hennrikus DJ, Lando HA, Kendall DM. Integrated tobacco cessation counseling in a diabetes self-management training program: a randomized trial of diabetes and reduction of tobacco. Diabetes Educ. 2006;32(4):562-70.

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

7 APPENDICES

7.1 Appendix 1 References related to the included studies
7.2 Appendix 2 Inclusion criteria A
7.3 Appendix 3 Inclusion criteria B
7.4 Appendix 4 Inclusion criteria C
7.5 Appendix 5 Inclusion criteria D
7.6 Appendix 6 Inclusion criteria E
7.7 Appendix 7 Inclusion criteria F
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7.9 Appendix 9 Review articles
7.10 Appendix 10 Excluded articles

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7.1 Appendix 1 References of included studies

Articles were assigned (included, excluded) according the following criteria:

0 Excluded (not belonging to at least one category A - G or R)

A Association to CVD

B Association to respiratory diseases

C Association to other diseases

D Levels in smokers and non-smokers

E Dose-response relationship to smoking intensity

F Effect of smoking cessation

G Effect of switching to MRTPs or other products

R Review article

Source 1: Articles derived from monographs: 4 References [1-4]

Source 2: Articles from PubMed Search 1(Reviews on HbA1ctin): 79 References [5-83]

Source 3: Articles derived from PubMed Search 2 (smoking-related studies on HbA1c: 52 References [37, 84-134]

Source 4: Articles derived from PubMed Search 3 (association between HbA1c and cardiovascular diseases): 29 References [8, 19, 72, 89, 103, 107, 119, 135-156]

Source 5: Articles derived from PubMed Search 4 (association between HbA1c and respiratory diseases): 4 References [157-160]

Source 6: Articles derived from PubMed Search 4 (association between HbA1c and other diseases, including cancer): 12 References [92, 107, 113, 139, 161-168]

Source 7: Articles derived from citations in publications from Sources 1 - 6: 35 References [169-203]

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List of all retrieved references

(1) Bott, U., Jorgens, V., Grusser, M., Bender, R., Muhlhauser, I., and Berger, M. (1994) Predictors of glycaemic control in type 1 diabetic patients after participation in an intensified treatment and teaching programme. *Diabet Med.*, *11*, 362-371. **A**

(2) Eliasson, B. (2003) Cigarette smoking and diabetes. *Prog Cardiovasc Dis.*, *45*, 405-413. **A, R**

(3) Lundman, B. M., Asplund, K., and Norberg, A. (1990) Smoking and metabolic control in patients with insulin-dependent diabetes mellitus. *J Intern Med.*, *227*, 101-106. **A**

(4) Sargeant, L. A., Khaw, K. T., Bingham, S., Day, N. E., Luben, R. N., Oakes, S., Welch, A., and Wareham, N. J. (2001) Cigarette smoking and glycaemia: the EPIC-Norfolk Study. European Prospective Investigation into Cancer. *Int J Epidemiol.*, *30*, 547-554. **D**

(5) Ahmad, J., and Rafat, D. (2013) HbA1c and iron deficiency: a review. *Diabetes Metab Syndr.*, *7*, 118-122. doi: 110.1016/j.dsx.2013.1002.1004. Epub 2013 Mar 1015. **R**

(6) Aoki, Y. (2013) [Approach to the changes of HbA1c notation in health checkups]. *Rinsho Byori.*, *61*, 607-611. **02**

(7) Barth, J. H., Marshall, S. M., and Watson, I. D. (2008) Consensus meeting on reporting glycated haemoglobin (HbA1c) and estimated average glucose (eAG) in the UK: report to the National Director for Diabetes, Department of Health. *Diabet Med.*, *25*, 381-382. doi: 310.1111/j.1464-5491.2008.02436.x. **R**

(8) Benhalima, K., Standl, E., and Mathieu, C. (2011) The importance of glycemic control: how low should we go with HbA1c? Start early, go safe, go low. *J Diabetes Complications.*, *25*, 202-207. doi: 210.1016/j.jdiacomp.2010.1003.1002. Epub 2010 May 1011. **R, A**

(9) Bordas-Fonfrede, M., Selam, J., Goudable, J., Thivolet, C., Vialettes, B., Chapelle, J., Drouin, P., Hue, G., Levy-Marchal, C., Slama, G., and Gillery, P. (2000) [Considerations on delocalized HbA1c assays]. *Diabetes Metab.*, *26*, 508-512. **01**

(10) Bottermann, P. (2009) [HbA1c 8.5% in elderly people with diabetes: is it good enough?]. *MMW Fortschr Med.*, *151*, 38-39. **03**

(11) Bryskiewicz, M. E., and Majkowska, L. (2011) [Aspects of the standardization of glycated hemoglobin (HbA1c) measurement]. *Pol Merkur Lekarski.*, *30*, 155-159. **01**

(12) Bryskiewicz, M. E., and Majkowska, L. (2011) [Glycated hemoglobin (HbA1c) as a standard diagnostic criterium for diabetes?]. *Pol Merkur Lekarski.*, *30*, 150-154. **02**

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

(13) Carter, P., Achana, F., Troughton, J., Gray, L. J., Khunti, K., and Davies, M. J. (2014) A Mediterranean diet improves HbA1c but not fasting blood glucose compared to alternative dietary strategies: a network meta-analysis. *J Hum Nutr Diet.*, *27*, 280-297. doi: 210.1111/jhn.12138. Epub 12013 Jun 12122. **R**

(14) Casparie, A. F., and Miedema, K. (1980) [HBA1c and diabetes mellitus]. *Ned Tijdschr Geneeskd.*, *124*, 930-934. **02**

(15) Chetty, V. T., Almulla, A., Odueyungbo, A., and Thabane, L. (2008) The effect of continuous subcutaneous glucose monitoring (CGMS) versus intermittent whole blood finger-stick glucose monitoring (SBGM) on hemoglobin A1c (HBA1c) levels in Type I diabetic patients: a systematic review. *Diabetes Res Clin Pract.*, *81*, 79-87. doi: 10.1016/j.diabres.2008.1002.1014. Epub 2008 Apr 1015. **R**

(16) Cohen, R. M., and Smith, E. P. (2008) Frequency of HbA1c discordance in estimating blood glucose control. *Curr Opin Clin Nutr Metab Care.*, *11*, 512-517. doi: 510.1097/MCO.1090b1013e32830467bd. **R**

(17) DeFronzo, R. A., Stonehouse, A. H., Han, J., and Wintle, M. E. (2010) Relationship of baseline HbA1c and efficacy of current glucose-lowering therapies: a meta-analysis of randomized clinical trials. *Diabet Med.*, *27*, 309-317. doi: 310.1111/j.1464-5491.2010.02941.x. **R**

(18) Doggrell, S. A., and Warot, S. (2014) The association between the measurement of adherence to anti-diabetes medicine and the HbA1c. *Int J Clin Pharm.*, *36*, 488-497. doi: 410.1007/s11096-11014-19929-11096. Epub 12014 Mar 11022. **02**

(19) Dorchy, H. (2015) One center in Brussels has consistently had the lowest HbA1c values in the 4 studies (1994-2009) by the Hvidoere International Study Group on Childhood Diabetes: What are the "recipes"? *World J Diabetes.*, *6*, 1-7. doi: 10.4239/wjd.v4236.i4231.4231. **01**

(20) Esposito, K., Chiodini, P., Bellastella, G., Maiorino, M. I., and Giugliano, D. (2012) Proportion of patients at HbA1c target <7% with eight classes of antidiabetic drugs in type 2 diabetes: systematic review of 218 randomized controlled trials with 78 945 patients. *Diabetes Obes Metab.*, *14*, 228-233. doi: 210.1111/j.1463-1326.2011.01512.x. Epub 02011 Nov 01513. **02**

(21) Florkowski, C. (2013) HbA1c as a Diagnostic Test for Diabetes Mellitus - Reviewing the Evidence. *Clin Biochem Rev.*, *34*, 75-83. **R**

(22) Gillery, P. (2000) [Strengths and limitations of Hba1c determination. The point of view of the biologist]. *Journ Annu Diabetol Hotel Dieu*, 195-201. **R**

(23) Gillery, P. (2005) [Where are we now with the quantitation of HbA1c?]. *Journ Annu Diabetol Hotel Dieu*, 125-129. **R**

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

(24) Giugliano, D., Maiorino, M., Bellastella, G., Chiodini, P., and Esposito, K. (2011) Relationship of baseline HbA1c, HbA1c change and HbA1c target of < 7% with insulin analogues in type 2 diabetes: a meta-analysis of randomised controlled trials. *Int J Clin Pract.*, *65*, 602-612. doi: 610.1111/j.1742-1241.2010.02619.x. **02**

(25) Giugliano, D., Maiorino, M. I., Bellastella, G., Chiodini, P., and Esposito, K. (2011) Multiple HbA1c targets and insulin analogues in type 2 diabetes: a systematic review. *J Diabetes Complications.*, *25*, 275-281. doi: 210.1016/j.jdiacomp.2011.1003.1005. Epub 2011 May 1020. **02**

(26) Heinemann, L., and Freckmann, G. (2015) Quality of HbA1c Measurement in the Practice: The German Perspective. *J Diabetes Sci Technol*, *17*, 1932296815572254. **R**

(27) Higgins, T. (2013) HbA1c for screening and diagnosis of diabetes mellitus. *Endocrine.*, *43*, 266-273. doi: 210.1007/s12020-12012-19768-y. Epub 12012 Aug 12021. **R**

(28) Hirst, J. A., Farmer, A. J., Dyar, A., Lung, T. W., and Stevens, R. J. (2013) Estimating the effect of sulfonylurea on HbA1c in diabetes: a systematic review and meta-analysis. *Diabetologia.*, *56*, 973-984. doi: 910.1007/s00125-00013-02856-00126. Epub 02013 Mar 00115. **02**

(29) Hoelzel, W., and Miedema, K. (1996) Development of a reference system for the international standardization of HbA1c/glycohemoglobin determinations. *J Int Fed Clin Chem*, *1996 Jun;8*, 62-64. **R**

(30) Jazet, I. M., and Meinders, A. E. (2009) Glucoregulation in type 2 diabetes: the lower the better? Glycosylated HbA1c of 6.5% seems to be the limit. *Eur J Intern Med.*, *20*, 232-235. doi: 210.1016/j.ejim.2008.1008.1002. Epub 2008 Sep 1014. **R**

(31) Jones, A., Gladstone, B. P., Lubeck, M., Lindekilde, N., Upton, D., and Vach, W. (2014) Motivational interventions in the management of HbA1c levels: a systematic review and meta-analysis. *Prim Care Diabetes.*, *8*, 91-100. doi: 110.1016/j.pcd.2014.1001.1009. Epub 2014 Feb 1010. **02**

(32) Juarez, D. T., Demaris, K. M., Goo, R., Mnatzaganian, C. L., and Wong Smith, H. (2014) Significance of HbA1c and its measurement in the diagnosis of diabetes mellitus: US experience. *Diabetes Metab Syndr Obes.*, *7:487-94.*, 10.2147/DMSO.S39092. eCollection 32014. **R**

(33) Kashiwagi, A. (2013) [Development of the HbA1c international standardization of HbA1c measurement in Japan Diabetes Society]. *Rinsho Byori.*, *61*, 585-593. **01**

(34) Kawahara, R. (1998) [Glycohemoglobin (HbA1c, HbA1)]. *Nihon Rinsho.*, *56*, 55-58. **01**

(35) Kawahara, R. (1999) [Glycohemoglobin (HbA1c, HbA1)]. *Nihon Rinsho.*, *57*, 615-617. **01**

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(36) Kirk, J. K., D'Agostino, R. B., Jr., Bell, R. A., Passmore, L. V., Bonds, D. E., Karter, A. J., and Narayan, K. M. (2006) Disparities in HbA1c levels between African-American and non-Hispanic white adults with diabetes: a meta-analysis. *Diabetes Care.*, *29*, 2130-2136. **R**

(37) Kowall, B., and Rathmann, W. (2013) HbA1c for diagnosis of type 2 diabetes. Is there an optimal cut point to assess high risk of diabetes complications, and how well does the 6.5% cutoff perform? *Diabetes Metab Syndr Obes.*, *6:477-91.*, 10.2147/DMSO.S39093. **R, A**

(38) Kurukulasuriya, L. R., and Sowers, J. R. (2010) Therapies for type 2 diabetes: lowering HbA1c and associated cardiovascular risk factors. *Cardiovasc Diabetol.*, *9:45.*, 10.1186/1475-2840-1189-1145. **R, A**

(39) Lai, L. C. (2008) Global standardisation of HbA1c. *Malays J Pathol.*, *30*, 67-71. **R**

(40) Landgraf, R. (2004) The relationship of postprandial glucose to HbA1c. *Diabetes Metab Res Rev.*, *20*, S9-S12. **R**

(41) Landgraf, R. (2006) [HbA1c--the gold standard in the assessment of diabetes treatment?]. *Dtsch Med Wochenschr.*, *131*, S243-246. **R**

(42) Lapolla, A., Dalfra, M. G., and Fedele, D. (2010) Pregnancy complicated by diabetes: what is the best level of HbA1c for conception? *Acta Diabetol.*, *47*, 187-192. doi: 110.1007/s00592-00010-00199-z. Epub 02010 May 00526. **03**

(43) LaSalle, J. R. (2010) Reaching HbA1c goals with saxagliptin in combination with other oral antidiabetic drugs. *Postgrad Med.*, *122*, 144-152. doi: 110.3810/pgm.2010.3801.2108. **0**

(44) Lefebvre, P. (2000) [Strengths and limitations of Hba1c determination: the point of view of the clinician]. *Journ Annu Diabetol Hotel Dieu*, 203-210. **R**

(45) Letourneau, J., Bui, H., Schricker, T., and Hatzakorzian, R. (2013) HbA1c: a prognostic biomarker in the surgical and critically ill patient population. *J Cardiothorac Vasc Anesth.*, *27*, 760-764. doi: 710.1053/j.jvca.2012.1006.1030. Epub 2012 Aug 1031. **R, A**

(46) Lieber, B. A., Taylor, B., Appelboom, G., Prasad, K., Bruce, S., Yang, A., Bruce, E., Christophe, B., and Connolly, E. S., Jr. (2015) Meta-analysis of telemonitoring to improve HbA1c levels: Promise for stroke survivors. *J Clin Neurosci*, *16*, 00706-00701. **02**

(47) Liew, A. K., Punnanithinont, N., Lee, Y. C., and Yang, J. (2013) Effect of non-surgical periodontal treatment on HbA1c: a meta-analysis of randomized controlled trials. *Aust Dent J.*, *58*, 350-357. doi: 310.1111/adj.12091. **R, C**

(48) Little, R. R., and Rohlfing, C. L. (2013) The long and winding road to optimal HbA1c measurement. *Clin Chim Acta.*, *418:63-71.*, 10.1016/j.cca.2012.1012.1026. Epub 2013 Jan 1011. **R**

Confidentiality Statement

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(49) Little, R. R., and Sacks, D. B. (2009) HbA1c: how do we measure it and what does it mean? *Curr Opin Endocrinol Diabetes Obes.*, *16*, 113-118. doi: 110.1097/MED.1090b1013e328327728d. **R**

(50) Manley, S. E. (2008) Estimated average glucose derived from HbA1c eAG: report from European Association for the Study of Diabetes (EASD), Amsterdam 2007. *Diabet Med.*, *25*, 126-128. doi: 110.1111/j.1464-5491.2008.02383.x. **R**

(51) Marre, M. (1998) [Which HbA1c to look at?]. *Journ Annu Diabetol Hotel Dieu*, 249-256. **R**

(52) Marshall, S. M., and Barth, J. H. (2000) Standardization of HbA1c measurements--a consensus statement. *Diabet Med.*, *17*, 5-6. **R**

(53) Mavian, A. A., Miller, S., and Henry, R. R. (2010) Managing type 2 diabetes: balancing HbA1c and body weight. *Postgrad Med.*, *122*, 106-117. doi: 110.3810/pgm.2010.3805.2148. **02**

(54) Moona, M. M., Smits, R., Kertesz, J., Meyer, A., and Mackler, L. (2014) Clinical inquiry: do complementary agents lower HbA1c when used with standard type 2 diabetes therapy? *J Fam Pract.*, *63*, 336-338. **02**

(55) Mostafa, S. A., Davies, M. J., Srinivasan, B. T., Carey, M. E., Webb, D., and Khunti, K. (2010) Should glycated haemoglobin (HbA1c) be used to detect people with type 2 diabetes mellitus and impaired glucose regulation? *Postgrad Med J.*, *86*, 656-662. doi: 610.1136/pgmj.2009.091215. Epub 092010 Oct 091218. **R**

(56) Ngiam, K. Y., Lee, W. J., Lee, Y. C., and Cheng, A. (2014) Efficacy of metabolic surgery on HbA1c decrease in type 2 diabetes mellitus patients with BMI <35 kg/m2--a review. *Obes Surg.*, *24*, 148-158. doi: 110.1007/s11695-11013-11112-y. **02**

(57) Nishio, Y. (2013) [New era of laboratory testing. Topics: II. Particulars; 1. Clinical laboratory test for diabetes: topics in HbA1c]. *Nihon Naika Gakkai Zasshi.*, *102*, 3110-3116. **02**

(58) Nitin, S. (2010) HbA1c and factors other than diabetes mellitus affecting it. *Singapore Med J.*, *51*, 616-622. **R**

(59) Oghagbon, E. K. (2014) Commentary: improving persistently elevated HbA1c in diabetes mellitus patients in Nigeria. *Ethn Dis.*, *24*, 502-507. **03**

(60) Osawa, H., Onuma, H., and Makino, H. (2005) [Combined use of fasting plasma glucose and HbA1c (as a screening test)]. *Nihon Rinsho.*, *63*, 390-393. **02**

(61) Procopiou, M. (2006) [HbA1c: review and recent developments]. *Rev Med Suisse*, *2006 May 31;2*, 1473-1474. **R**

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

(62) Punales, M. K., Geremia, C., Mondadori, P., Pickler, M., Fornari, A., and Tschiedel, B. (2008) [How the continuous glucose monitoring system can contribute to HbA1c interpretation in type 1 diabetes mellitus?]. *Arq Bras Endocrinol Metabol.*, *52*, 299-306. **R**

(63) Rafat, D., and Ahmad, J. (2012) HbA1c in pregnancy. *Diabetes Metab Syndr.*, *6*, 59-64. doi: 10.1016/j.dsx.2012.1005.1010. Epub 2012 Jun 1030. **03**

(64) Reynolds, T. M., Smellie, W. S., and Twomey, P. J. (2006) Glycated haemoglobin (HbA1c) monitoring. *BMJ.*, *333*, 586-588. **R**

(65) Rollins, K. E., Varadhan, K. K., Dhatariya, K., and Lobo, D. N. (2015) Systematic review of the impact of HbA1c on outcomes following surgery in patients with diabetes mellitus. *Clin Nutr*, *17*, 00082-00085. **R, C**

(66) Roszyk, L., Faye, B., Sapin, V., Somda, F., and Tauveron, I. (2007) Glycated haemoglobin (HbA1c): today and tomorrow. *Ann Endocrinol (Paris). 68*, 357-365. Epub 2007 Sep 2029. **R**

(67) Sato, A. (2014) [Indicators of glycemic control --hemoglobin A1c (HbA1c), glycated albumin (GA), and 1,5-anhydroglucitol (1,5-AG)]. *Rinsho Byori.*, *62*, 45-52. **02**

(68) Schnedl, W. J., Liebminger, A., Roller, R. E., Lipp, R. W., and Krejs, G. J. (2001) Hemoglobin variants and determination of glycated hemoglobin (HbA1c). *Diabetes Metab Res Rev.*, *17*, 94-98. **R**

(69) Seitz, P., Rosemann, T., Gensichen, J., and Huber, C. A. (2011) Interventions in primary care to improve cardiovascular risk factors and glycated haemoglobin (HbA1c) levels in patients with diabetes: a systematic review. *Diabetes Obes Metab.*, *13*, 479-489. doi: 410.1111/j.1463-1326.2010.01347.x. **R, A**

(70) Shima, K., and Kuwajima, M. (1998) [Standardization for glycohemoglobin (HbA1c) measurements and its evaluation]. *Nihon Rinsho.*, *56*, 59-67. **01**

(71) Stettler, C., Mueller, B., and Diem, P. (2000) [What you always wanted to know about HbA1c]. *Schweiz Med Wochenschr.*, *130*, 993-1005. **R**

(72) Sturm, G., Lamina, C., Zitt, E., Lhotta, K., Haider, F., Neyer, U., and Kronenberg, F. (2011) Association of HbA1c values with mortality and cardiovascular events in diabetic dialysis patients. The INVOR study and review of the literature. *PLoS One*, *6*, e20093. doi: 20010.21371/journal.pone.0020093. Epub 0022011 May 0020018. **R, A, C**

(73) Tahara, Y., and Shima, K. (2005) [Analysis of HbA1c and glycoalbumin for diagnosis of impaired glucose tolerance]. *Nihon Rinsho.*, *63*, 382-385. **02**

(74) ten Brinke, R., Dekker, N., de Groot, M., and Ikkersheim, D. (2008) Lowering HbA1c in type 2 diabetics results in reduced risk of coronary heart disease and all-cause mortality. *Prim Care Diabetes.*, *2*, 45-49. doi: 10.1016/j.pcd.2007.1012.1004. Epub 2008 Feb 1018. **R, A, C**

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

(75) Tennyson, C., Lee, R., and Attia, R. (2013) Is there a role for HbA1c in predicting mortality and morbidity outcomes after coronary artery bypass graft surgery? *Interact Cardiovasc Thorac Surg.*, *17*, 1000-1008. doi: 1010.1093/icvts/ivt1351. Epub 2013 Sep 1010. **R, A**

(76) Tominaga, M. (2002) [Hemoglobin A1c (HbA1c)]. *Nihon Rinsho.*, *60*, 405-409. **01**

(77) Tominaga, M. (2003) [Diabetes mellitus and HbA1c]. *Rinsho Byori.*, *51*, 586-591. **02**

(78) Toth, L., Szenasi, P., Kammerer, L., and Romics, L. (1990) [Correlation of thrombocyte reactivity and serum levels of HbA1c, cholesterol and creatinine in diabetes mellitus]. *Orv Hetil*, *1990 Feb 25;131*, 405-406. **02**

(79) Umpierre, D., Ribeiro, P. A., Kramer, C. K., Leitao, C. B., Zucatti, A. T., Azevedo, M. J., Gross, J. L., Ribeiro, J. P., and Schaan, B. D. (2011) Physical activity advice only or structured exercise training and association with HbA1c levels in type 2 diabetes: a systematic review and meta-analysis. *JAMA.*, *305*, 1790-1799. doi: 1710.1001/jama.2011.1576. **R, A, C**

(80) Valentine, W. J., Palmer, A. J., Nicklasson, L., Cobden, D., and Roze, S. (2006) Improving life expectancy and decreasing the incidence of complications associated with type 2 diabetes: a modelling study of HbA1c targets. *Int J Clin Pract.*, *60*, 1138-1145. **R**

(81) Weykamp, C. (2013) HbA1c: a review of analytical and clinical aspects. *Ann Lab Med.*, *33*, 393-400. doi: 310.3343/alm.2013.3333.3346.3393. Epub 2013 Oct 3317. **R**

(82) Yagame, M., Jinde, K., Suzuki, D., Saotome, N., Takano, H., Tanabe, R., Sato, H., Kurokawa, K., Sakai, H., Matsumae, M., Mase, H., and Harano, T. (1997) A diabetic case with hemoglobin J-Meerut and low HbA1C levels. *Intern Med.*, *36*, 351-356. **02**

(83) Yan, S., Liu, S., Zhao, Y., Zhang, W., Sun, X., Li, J., Jiang, F., Ju, J., Lang, N., Zhang, Y., Zhou, W., and Li, Q. (2013) Diagnostic accuracy of HbA1c in diabetes between Eastern and Western. *Eur J Clin Invest.*, *43*, 716-726. doi: 710.1111/eci.12098. Epub 12013 May 12092. **02**

(84) Aggarwal, J., and Kumar, M. (2014) Prevalence of Microalbuminuria among Rural North Indian Population with Diabetes Mellitus and its Correlation with Glycosylated Haemoglobin and Smoking. *J Clin Diagn Res.*, *8*, CC11-13. doi: 10.7860/JCDR/2014/9758.4613. Epub 2014 Jul 7820. **C**

(85) Arai, K., Hirao, K., Yamauchi, M., Kobayashi, M., and Kashiwagi, A. (2013) Short duration of diabetes and disuse of sulfonylurea have any association with insulin cessation of the patients with type 2 diabetes in a clinical setting in Japan (JDDM 30). *Endocr J*, *60*, 305-310. Epub 2012 Nov 2010. **02**

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

(86) Borg, R., Vistisen, D., Witte, D. R., and Borch-Johnsen, K. (2010) Comparing risk profiles of individuals diagnosed with diabetes by OGTT and HbA1c The Danish Inter99 study. *Diabet Med.*, *27*, 906-910. doi: 910.1111/j.1464-5491.2010.03034.x. **D, A**

(87) Cederholm, J., Zethelius, B., Nilsson, P. M., Eeg-Olofsson, K., Eliasson, B., and Gudbjornsdottir, S. (2009) Effect of tight control of HbA1c and blood pressure on cardiovascular diseases in type 2 diabetes: an observational study from the Swedish National Diabetes Register (NDR). *Diabetes Res Clin Pract.*, *86*, 74-81. doi: 10.1016/j.diabres.2009.1007.1003. Epub 2009 Aug 1012. **A, D**

(88) Choi, Y. J., Park, J. S., Kim, U., Lee, S. H., Son, J. W., Shin, D. G., Kim, Y. J., Jeong, M. H., Ahn, Y. K., Cho, M. C., Bae, J. W., Kim, C. J., Cho, J. M., Han, K. R., and Lee, J. H. (2013) Changes in smoking behavior and adherence to preventive guidelines among smokers after a heart attack. *J Geriatr Cardiol.*, *10*, 146-150. doi: 110.3969/j.issn.1671-5411.2013.3902.3006. **F, A**

(89) Cohen, H. W., Crandall, J. P., Hailpern, S. M., and Billett, H. H. (2008) Aspirin resistance associated with HbA1c and obesity in diabetic patients. *J Diabetes Complications.*, *22*, 224-228. doi: 210.1016/j.jdiacomp.2007.1005.1002. Epub 2008 Apr 1016. **03**

(90) Diez-Espino, J., Buil-Cosiales, P., Serrano-Martinez, M., Toledo, E., Salas-Salvado, J., and Martinez-Gonzalez, M. A. (2011) Adherence to the Mediterranean diet in patients with type 2 diabetes mellitus and HbA1c level. *Ann Nutr Metab*, *58*, 74-78. doi: 10.1159/000324718. Epub 000322011 Mar 000324724. **D, A**

(91) Fan, H. Q., Tang, W., Wang, Z. X., Wang, S. J., Qin, Y. H., Fu, Q., Gao, Y., Sun, M., Zhang, M., Zhou, H. W., and Yang, T. (2013) Association of serum uric acid with 2-hour postload glucose in Chinese with impaired fasting plasma glucose and/or HbA1c. *PLoS One.*, *8*, e67759. doi: 67710.61371/journal.pone.0067759. Print 0062013. **02**

(92) Fan, Y., Huang, X. D., Zhang, H., Wu, J., Zhang, X. X., and Luo, H. S. (2014) Association between serum HbA1c levels and adenomatous polyps in patients with the type 2 diabetes mellitus. *Minerva Endocrinol*, *8*, 8. **C**

(93) Gerber, P. A., Locher, R., Schmid, B., Spinas, G. A., and Lehmann, R. (2013) Smoking is associated with impaired long-term glucose metabolism in patients with type 1 diabetes mellitus. *Nutr Metab Cardiovasc Dis.*, *23*, 102-108. doi: 110.1016/j.numecd.2011.1008.1007. Epub 2011 Nov 1025. **D**

(94) Govan, L., Maietti, E., Torsney, B., Wu, O., Briggs, A., Colhoun, H. M., Fischbacher, C. M., Leese, G. P., McKnight, J. A., Morris, A. D., Sattar, N., Wild, S. H., and Lindsay, R. S. (2012) The effect of deprivation and HbA1c on admission to hospital for diabetic ketoacidosis in type 1 diabetes. *Diabetologia.*, *55*, 2356-2360. Epub 2012 Jun 2326. **03**

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(95) Halmai, R., Degrell, P., Szijarto, I. A., Matyas, V., Molnar, G. A., Kovacs, T., and Wittmann, I. (2013) Smoking as the potential link between Kimmelstiel-Wilson lesion and non-diabetic nodular glomerulosclerosis in male patients - a single center retrospective study. *Clin Nephrol.*, *80*, 23-28. doi: 10.5414/CN107812. **01**

(96) Hara, M., Higaki, Y., Taguchi, N., Shinchi, K., Morita, E., Naito, M., Hamajima, N., Takashima, N., Suzuki, S., Nakamura, A., Ohnaka, K., Uemura, H., Nishida, H., Hosono, S., Mikami, H., Kubo, M., and Tanaka, H. (2012) Effect of the PPARG2 Pro12Ala polymorphism and clinical risk factors for diabetes mellitus on HbA1c in the Japanese general population. *J Epidemiol*, *22*, 523-531. doi: 510.2188/jea.JE20120078. Epub 20122012 Sep 20120022. **03**

(97) Hayashida, H., Kawasaki, K., Yoshimura, A., Kitamura, M., Furugen, R., Nakazato, M., Takamura, N., Hara, Y., Maeda, T., and Saito, T. (2009) Relationship between periodontal status and HbA1c in nondiabetics. *J Public Health Dent.*, *69*, 204-206. doi: 210.1111/j.1752-7325.2009.00122.x. **A, D**

(98) Herbert, M. S., Varley, A. L., Andreae, S. J., Goodin, B. R., Bradley, L. A., and Safford, M. M. (2013) Association of pain with HbA1c in a predominantly black population of community-dwelling adults with diabetes: a cross-sectional analysis. *Diabet Med.*, *30*, 1466-1471. doi: 1410.1111/dme.12264. Epub 12013 Jul 12219. **C**

(99) Hodge, P. J., Robertson, D., Paterson, K., Smith, G. L., Creanor, S., and Sherriff, A. (2012) Periodontitis in non-smoking type 1 diabetic adults: a cross-sectional study. *J Clin Periodontol.*, *39*, 20-29. doi: 10.1111/j.1600-1051X.2011.01791.x. Epub 02011 Oct 01731. **C**

(100) Hofer, S. E., Rosenbauer, J., Grulich-Henn, J., Naeke, A., Frohlich-Reiterer, E., and Holl, R. W. (2009) Smoking and metabolic control in adolescents with type 1 diabetes. *J Pediatr.*, *154*, 20-23.e21. doi: 10.1016/j.jpeds.2008.1007.1052. Epub 2008 Sep 1019. **D**

(101) Hou, R. L., Zhou, H. H., Chen, X. Y., Wang, X. M., Shao, J., and Zhao, Z. Y. (2014) Effect of maternal lipid profile, C-peptide, insulin, and HBA1c levels during late pregnancy on large-for-gestational age newborns. *World J Pediatr.*, *10*, 175-181. doi: 110.1007/s12519-12014-10488-12517. Epub 12014 May 12517. **C**

(102) Hou, X., Wang, C., Wang, S., Yang, W., Ma, Z., Wang, Y., Li, C., Li, M., Zhang, X., Zhao, X., Sun, Y., Song, J., Lin, P., Liang, K., Gong, L., Wang, M., Liu, F., Li, W., Yan, F., Yang, J., Wang, L., Tian, M., Liu, J., Zhao, R., Chen, S., and Chen, L. (2014) Fluctuation between fasting and 2-H postload glucose state is associated with glomerular hyperfiltration in newly diagnosed diabetes patients with HbA1c < 7%. *PLoS One.*, *9*, e111173. doi: 111110.111371/journal.pone.0111173. eCollection 0112014. **02**

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(103) Jansen, H., Stolk, R. P., Nolte, I. M., Kema, I. P., Wolffenbuttel, B. H., and Snieder, H. (2013) Determinants of HbA1c in nondiabetic Dutch adults: genetic loci and clinical and lifestyle parameters, and their interactions in the Lifelines Cohort Study. *J Intern Med.*, *273*, 283-293. doi: 210.1111/joim.12010. Epub 12012 Dec 12015. **A, D**

(104) Javed, F., Al-Kheraif, A. A., Al Amri, M. D., Alshehri, M., Vohra, F., Al-Askar, M., Malmstrom, H., and Romanos, G. E. (2015) Periodontal Status and Whole Salivary Cytokine Profile Among Smokers and Never-Smokers With and Without Prediabetes. *J Periodontol*, *12*, 1-15. **03**

(105) Kerr, D., Partridge, H., Knott, J., and Thomas, P. W. (2011) HbA1c 3 months after diagnosis predicts premature mortality in patients with new onset type 2 diabetes. *Diabet Med.*, *28*, 1520-1524. doi: 1510.1111/j.1464-5491.2011.03443.x. **D, C**

(106) Kotani, K., Sakane, N., Miyamoto, M., Yamada, K., and Taniguchi, N. (2010) Influence of smoking habits on the GA/HbA1c ratio in patients with type 1 diabetes mellitus. *Med Princ Pract*, *19*, 415-417. doi: 410.1159/000316385. Epub 000312010 Jul 000316314. **D**

(107) Levitan, E. B., Liu, S., Stampfer, M. J., Cook, N. R., Rexrode, K. M., Ridker, P. M., Buring, J. E., and Manson, J. E. (2008) HbA1c measured in stored erythrocytes and mortality rate among middle-aged and older women. *Diabetologia.*, *51*, 267-275. Epub 2007 Nov 2028. **C**

(108) Lipska, K. J., Inzucchi, S. E., Van Ness, P. H., Gill, T. M., Kanaya, A., Strotmeyer, E. S., Koster, A., Johnson, K. C., Goodpaster, B. H., Harris, T., and De Rekeneire, N. (2013) Elevated HbA1c and fasting plasma glucose in predicting diabetes incidence among older adults: are two better than one? *Diabetes Care.*, *36*, 3923-3929. doi: 3910.2337/dc3912-2631. Epub 2013 Oct 3917. **02**

(109) M, M., Sembian, U., Babitha, N, E., and K, M. (2014) Study of Auditory, Visual Reaction Time and Glycemic Control (HBA1C) in Chronic Type II Diabetes Mellitus. *J Clin Diagn Res.*, *8*, BC11-13. doi: 10.7860/JCDR/2014/8906.4865. Epub 2014 Sep 7820. **A**

(110) Madden, T. E., Herriges, B., Boyd, L. D., Laughlin, G., Chiodo, G., and Rosenstein, D. (2008) Alterations in HbA1c following minimal or enhanced non-surgical, non-antibiotic treatment of gingivitis or mild periodontitis in type 2 diabetic patients: a pilot trial. *J Contemp Dent Pract.*, *9*, 9-16. **02**

(111) Melin, E. O., Thunander, M., Landin-Olsson, M., Hillman, M., and Thulesius, H. O. (2014) Depression, smoking, physical inactivity and season independently associated with midnight salivary cortisol in type 1 diabetes. *BMC Endocr Disord.*, *14:75.*, 10.1186/1472-6823-1114-1175. **C**

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(112) Melin, E. O., Thunander, M., Svensson, R., Landin-Olsson, M., and Thulesius, H. O. (2013) Depression, obesity, and smoking were independently associated with inadequate glycemic control in patients with type 1 diabetes. *Eur J Endocrinol.*, *168*, 861-869. doi: 810.1530/EJE-1513-0137. Print 2013 Jun. **D, C**

(113) Miao Jonasson, J., Cederholm, J., Eliasson, B., Zethelius, B., Eeg-Olofsson, K., and Gudbjornsdottir, S. (2012) HbA1C and cancer risk in patients with type 2 diabetes--a nationwide population-based prospective cohort study in Sweden. *PLoS One*, *7*, e38784. doi: 38710.31371/journal.pone.0038784. Epub 0032012 Jun 0038714. **C**

(114) Nakhjavani, M., Esteghamati, A., Esfahanian, F., Ghanei, A., Rashidi, A., and Hashemi, S. (2008) HbA1c negatively correlates with LCAT activity in type 2 diabetes. *Diabetes Res Clin Pract.*, *81*, 38-41. doi: 10.1016/j.diabres.2008.1001.1018. Epub 2008 May 1015. **03**

(115) No, J. I., Yang, J. Y., Hyun, H. J., Yeon, C. S., and Choi, H. J. (2013) Factors Associated with Serum Levels of Carcinoembryonic Antigen in Healthy Non-smokers. *Korean J Fam Med.*, *34*, 413-419. doi: 410.4082/kjfm.2013.4034.4086.4413. Epub 2013 Nov 4025. **C**

(116) Ohkuma, T., Iwase, M., Fujii, H., Kaizu, S., Ide, H., Jodai, T., Kikuchi, Y., Idewaki, Y., Hirakawa, Y., Nakamura, U., and Kitazono, T. (2015) Dose- and time-dependent association of smoking and its cessation with glycemic control and insulin resistance in male patients with type 2 diabetes mellitus: the fukuoka diabetes registry. *PLoS One.*, *10*, e0122023. doi: 0122010.0121371/journal.pone.0122023. eCollection 0122015. **D, E, F**

(117) Orban, T., Bundy, B., Becker, D. J., Dimeglio, L. A., Gitelman, S. E., Goland, R., Gottlieb, P. A., Greenbaum, C. J., Marks, J. B., Monzavi, R., Moran, A., Peakman, M., Raskin, P., Russell, W. E., Schatz, D., Wherrett, D. K., Wilson, D. M., Krischer, J. P., and Skyler, J. S. (2014) Costimulation modulation with abatacept in patients with recent-onset type 1 diabetes: follow-up 1 year after cessation of treatment. *Diabetes Care.*, *37*, 1069-1075. doi: 1010.2337/dc1013-0604. Epub 2013 Dec 1062. **02**

(118) Power, C., Atherton, K., and Thomas, C. (2010) Maternal smoking in pregnancy, adult adiposity and other risk factors for cardiovascular disease. *Atherosclerosis.*, *211*, 643-648. doi: 610.1016/j.atherosclerosis.2010.1003.1015. Epub 2010 Mar 1016. **D, A**

(119) Qie, L. Y., Sun, J. P., Ning, F., Pang, Z. C., Gao, W. G., Ren, J., Nan, H. R., Zhang, L., and Qiao, Q. (2014) Cardiovascular risk profiles in relation to newly diagnosed type 2 diabetes diagnosed by either glucose or HbA1c criteria in Chinese adults in Qingdao, China. *Diabet Med.*, *31*, 920-926. doi: 910.1111/dme.12498. Epub 12014 Jun 12492. **A, D**

Confidentiality Statement

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(120) Sanz, C. M., Ruidavets, J. B., Bongard, V., Marquie, J. C., Hanaire, H., Ferrieres, J., and Andrieu, S. (2013) Relationship between markers of insulin resistance, markers of adiposity, HbA1c, and cognitive functions in a middle-aged population-based sample: the MONA LISA study. *Diabetes Care.*, *36*, 1512-1521. doi: 1510.2337/dc1512-1017. Epub 2012 Dec 1528. **D, C**

(121) Schwab, K. O., Doerfer, J., Hallermann, K., Krebs, A., Schorb, E., Krebs, K., and Winkler, K. (2008) Marked smoking-associated increase of cardiovascular risk in childhood type 1 diabetes. *Int J Adolesc Med Health.*, *20*, 285-292. **A, D**

(122) Shah, A. D., Fox, R. K., and Rushakoff, R. J. (2014) Falsely Decreased HbA1c in a Type 2 Diabetic Patient Treated with Dapsone. *Endocr Pract.*, *20*, e229-232. doi: 210.4158/EP14291.CR. **02**

(123) Siddiqui, A. A., Maddur, H., Naik, S., and Cryer, B. (2008) The association of elevated HbA1c on the behavior of adenomatous polyps in patients with type-II diabetes mellitus. *Dig Dis Sci.*, *53*, 1042-1047. Epub 2007 Oct 1016. **03**

(124) Soulimane, S., Simon, D., Herman, W. H., Lange, C., Lee, C. M., Colagiuri, S., Shaw, J. E., Zimmet, P. Z., Magliano, D., Ferreira, S. R., Dong, Y., Zhang, L., Jorgensen, T., Tuomilehto, J., Mohan, V., Christensen, D. L., Kaduka, L., Dekker, J. M., Nijpels, G., Stehouwer, C. D., Lantieri, O., Fujimoto, W. Y., Leonetti, D. L., McNeely, M. J., Borch-Johnsen, K., Boyko, E. J., Vistisen, D., and Balkau, B. (2014) HbA1c, fasting and 2 h plasma glucose in current, ex- and never-smokers: a meta-analysis. *Diabetologia.*, *57*, 30-39. doi: 10.1007/s00125-00013-03058-y. Epub 02013 Sep 00125. **D**

(125) Suchitra, M. R., Jaiganesh, K., and Parthasarathy, S. (2013) Diabetic Profile-Screening of HBA1C - A Random Community Assessment. *J Clin Diagn Res.*, *7*, 2200-2202. doi: 2210.7860/JCDR/2013/5690.3470. Epub 2013 Oct 2205. **D, A**

(126) Suljic, E., Kulasin, I., and Alibegovic, V. (2013) Assessment of Diabetic Polyneuropathy in Inpatient Care: Fasting Blood Glucose, HbA1c, Electroneuromyography and Diabetes Risk Factors. *Acta Inform Med*, *21*, 123-126. doi: 110.5455/aim.2013.5421.5123-5126. **02**

(127) Sun, Y., Wang, C., Yang, W., Wang, Y., Zhang, X., Ma, Z., Song, J., Lin, P., Liang, K., Ma, A., Zheng, H., Wu, J., Gong, L., Wang, M., Liu, F., Li, W., Yan, F., Yang, J., Wang, L., Tian, M., Liu, J., Zhao, R., Hou, X., and Chen, L. (2015) Fasting blood glucose, but not 2-h postload blood glucose or HbA1c, is associated with mild decline in estimated glomerular filtration rate in healthy Chinese. *Int Urol Nephrol.*, *47*, 147-152. doi: 110.1007/s11255-11014-10880-11251. Epub 12014 Dec 11211. **02**

(128) Susanto, H., Nesse, W., Dijkstra, P. U., Hoedemaker, E., van Reenen, Y. H., Agustina, D., Vissink, A., and Abbas, F. (2012) Periodontal inflamed surface area and C-reactive protein as predictors of HbA1c: a study in Indonesia. *Clin Oral Investig.*, *16*, 1237-1242. doi: 1210.1007/s00784-00011-00621-00780. Epub 02011 Oct 00720. **D, C**

Confidentiality Statement

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(129) Uruska, A., Araszkiewicz, A., Uruski, P., and Zozulinska-Ziolkiewicz, D. (2014) Higher risk of microvascular complications in smokers with type 1 diabetes despite intensive insulin therapy. *Microvasc Res.*, *92:79-84.*, 10.1016/j.mvr.2014.1001.1002. Epub 2014 Jan 1012. **D, A**

(130) Vlassopoulos, A., Lean, M. E., and Combet, E. (2013) Influence of smoking and diet on glycated haemoglobin and 'pre-diabetes' categorisation: a cross-sectional analysis. *BMC Public Health.*, *13:1013.*, 10.1186/1471-2458-1113-1013. **D, E**

(131) Wang, C., Song, J., Ma, Z., Yang, W., Li, C., Zhang, X., Hou, X., Sun, Y., Lin, P., Liang, K., Gong, L., Wang, M., Liu, F., Li, W., Yan, F., Yang, J., Wang, L., Tian, M., Liu, J., Zhao, R., and Chen, L. (2014) Fluctuation between fasting and 2-H postload glucose state is associated with chronic kidney disease in previously diagnosed type 2 diabetes patients with HbA1c >/= 7%. *PLoS One.*, *9*, e102941. doi: 102910.101371/journal.pone.0102941. eCollection 0102014. **A, C**

(132) Zhao, W., Katzmarzyk, P. T., Horswell, R., Wang, Y., Johnson, J., Heymsfield, S. B., Cefalu, W. T., Ryan, D. H., and Hu, G. (2013) HbA1c and lower-extremity amputation risk in low-income patients with diabetes. *Diabetes Care.*, *36*, 3591-3598. doi: 3510.2337/dc3513-0437. Epub 2013 Sep 3523. **A, C**

(133) Zhao, W., Katzmarzyk, P. T., Horswell, R., Wang, Y., Johnson, J., and Hu, G. (2014) HbA1c and heart failure risk among diabetic patients. *J Clin Endocrinol Metab.*, *99*, E263-267. doi: 210.1210/jc.2013-3325. Epub 2013 Jan 1211. **D, A**

(134) Zhao, W., Katzmarzyk, P. T., Horswell, R., Wang, Y., Johnson, J., and Hu, G. (2014) HbA1c and coronary heart disease risk among diabetic patients. *Diabetes Care.*, *37*, 428-435. doi: 410.2337/dc2313-1525. Epub 2013 Oct 2315. **D, A**

(135) (2013) HbA1c targets in type 2 diabetes: guidelines and evidence. *Drug Ther Bull.*, *51*, 42-45. doi: 10.1136/dtb.2013.1134.0172. Epub 2013 Apr 1133. **02**

(136) Andersson, C., van Gaal, L., Caterson, I. D., Weeke, P., James, W. P., Coutinho, W., Finer, N., Sharma, A. M., Maggioni, A. P., and Torp-Pedersen, C. (2012) Relationship between HbA1c levels and risk of cardiovascular adverse outcomes and all-cause mortality in overweight and obese cardiovascular high-risk women and men with type 2 diabetes. *Diabetologia.*, *55*, 2348-2355. doi: 2310.1007/s00125-00012-02584-00123. Epub 02012 May 00126. **A, C**

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

(137) Bernal-Lopez, M. R., Villalobos-Sanchez, A., Mancera-Romero, J., Jansen-Chaparro, S., Baca-Osorio, A. J., Lopez-Carmona, M. D., Tinahones, F. J., and Gomez-Huelgas, R. (2011) Why not use the HbA1c as a criterion of dysglycemia in the new definition of the metabolic syndrome? Impact of the new criteria in the prevalence of the metabolic syndrome in a Mediterranean urban population from Southern Europe (IMAP study. Multidisciplinary intervention in primary care). *Diabetes Res Clin Pract.*, *93*, e57-60. doi: 10.1016/j.diabres.2011.1002.1024. Epub 2011 Mar 1021. **02**

(138) Bouchi, R., Babazono, T., Mugishima, M., Yoshida, N., Nyumura, I., Toya, K., Hayashi, T., Hanai, K., Tanaka, N., Ishii, A., and Iwamoto, Y. (2012) Fluctuations in HbA1c are associated with a higher incidence of cardiovascular disease in Japanese patients with type 2 diabetes. *J Diabetes Investig.*, *3*, 148-155. doi: 110.1111/j.2040-1124.2011.00155.x. **A**

(139) Chamnan, P., Simmons, R. K., Khaw, K. T., Wareham, N. J., and Griffin, S. J. (2013) Change in HbA1c over 3 years does not improve the prediction of cardiovascular disease over and above HbA1c measured at a single time point. *Diabetologia.*, *56*, 1004-1011. doi: 1010.1007/s00125-00013-02854-00128. Epub 02013 Feb 00112. **A**

(140) Eeg-Olofsson, K., Cederholm, J., Nilsson, P. M., Zethelius, B., Svensson, A. M., Gudbjornsdottir, S., and Eliasson, B. (2010) New aspects of HbA1c as a risk factor for cardiovascular diseases in type 2 diabetes: an observational study from the Swedish National Diabetes Register (NDR). *J Intern Med.*, *268*, 471-482. doi: 410.1111/j.1365-2796.2010.02265.x. **A, C**

(141) Gao, L., Matthews, F. E., Sargeant, L. A., and Brayne, C. (2008) An investigation of the population impact of variation in HbA1c levels in older people in England and Wales: from a population based multi-centre longitudinal study. *BMC Public Health.*, *8:54.*, 10.1186/1471-2458-1188-1154. **A, C**

(142) Hernandez, D., Espejo-Gil, A., Bernal-Lopez, M. R., Mancera-Romero, J., Baca-Osorio, A. J., Tinahones, F. J., Armas-Padron, A. M., Ruiz-Esteban, P., Torres, A., and Gomez-Huelgas, R. (2013) Association of HbA1c and cardiovascular and renal disease in an adult Mediterranean population. *BMC Nephrol.*, *14:151.*, 10.1186/1471-2369-1114-1151. **A, C**

(143) Prabhavathi, K., Kunikullaya, U. K., and Goturu, J. (2014) Glycosylated Haemoglobin (HbA1c) - A Marker of Circulating Lipids in Type 2 Diabetic Patients. *J Clin Diagn Res.*, *8*, 20-23. doi: 10.7860/JCDR/2014/7742.3996. Epub 2014 Feb 7863. **A**

(144) Kesim, M., Tiryaki, A., Kadioglu, M., Muci, E., Kalyoncu, N. I., and Yaris, E. (2011) The effects of sertraline on blood lipids, glucose, insulin and HBA1C levels: A prospective clinical trial on depressive patients. *J Res Med Sci.*, *16*, 1525-1531. **02**

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

(145) Khaw, K. T. (2009) Elevated HbA1c level: a risk factor for cardiovascular disease mortality in patients with chronic heart failure? *Nat Clin Pract Endocrinol Metab.*, *5*, 130-131. doi: 110.1038/ncpendmet1069. **A**

(146) Kilpatrick, E. S., Rigby, A. S., and Atkin, S. L. (2008) Mean blood glucose compared with HbA1c in the prediction of cardiovascular disease in patients with type 1 diabetes. *Diabetologia.*, *51*, 365-371. Epub 2007 Nov 2027. **A**

(147) Lerstad, G., Brodin, E. E., Enga, K. F., Jorde, R., Schirmer, H., Njolstad, I., Svartberg, J., Braekkan, S. K., and Hansen, J. B. (2014) Hyperglycemia, assessed according to HbA1c , and future risk of venous thromboembolism: the Tromso study. *J Thromb Haemost*, *12*, 313-319. doi: 310.1111/jth.12498. **C**

(148) Lind, M., Tuomilehto, J., Uusitupa, M., Nerman, O., Eriksson, J., Ilanne-Parikka, P., Keinanen-Kiukaanniemi, S., Peltonen, M., Pivodic, A., and Lindstrom, J. (2014) The association between HbA1c, fasting glucose, 1-hour glucose and 2-hour glucose during an oral glucose tolerance test and cardiovascular disease in individuals with elevated risk for diabetes. *PLoS One.*, *9*, e109506. doi: 109510.101371/journal.pone.0109506. eCollection 0102014. **02**

(149) Luk, A. O., Ma, R. C., Lau, E. S., Yang, X., Lau, W. W., Yu, L. W., Chow, F. C., Chan, J. C., and So, W. Y. (2013) Risk association of HbA1c variability with chronic kidney disease and cardiovascular disease in type 2 diabetes: prospective analysis of the Hong Kong Diabetes Registry. *Diabetes Metab Res Rev.*, *29*, 384-390. doi: 310.1002/dmrr.2404. **A, C**

(150) Madar, A. A., Knutsen, K. V., Stene, L. C., Brekke, M., Meyer, H. E., and Lagerlov, P. (2014) Effect of vitamin D3 supplementation on glycated hemoglobin (HbA1c), fructosamine, serum lipids, and body mass index: a randomized, double-blinded, placebo-controlled trial among healthy immigrants living in Norway. *BMJ Open Diabetes Res Care.*, *2*, e000026. doi: 000010.001136/bmjdrc-002014-000026. eCollection 002014. **01**

(151) Nathan, D. M., McGee, P., Steffes, M. W., and Lachin, J. M. (2014) Relationship of glycated albumin to blood glucose and HbA1c values and to retinopathy, nephropathy, and cardiovascular outcomes in the DCCT/EDIC study. *Diabetes.*, *63*, 282-290. doi: 210.2337/db2313-0782. Epub 2013 Aug 2329. **A**

(152) Pacilli, A., De Cosmo, S., Trischitta, V., and Bacci, S. (2013) Role of relationship between HbA1c, fibrinogen and HDL-cholesterol on cardiovascular disease in patients with type 2 diabetes mellitus. *Atherosclerosis.*, *228*, 247-248. doi: 210.1016/j.atherosclerosis.2013.1002.1010. Epub 2013 Feb 1020. **A**

(153) van 't Riet, E., Rijkelijkhuizen, J. M., Alssema, M., Nijpels, G., Stehouwer, C. D., Heine, R. J., and Dekker, J. M. (2012) HbA1c is an independent predictor of non-fatal cardiovascular disease in a Caucasian population without diabetes: a 10-year follow-up of the Hoorn Study. *Eur J Prev Cardiol.*, *19*, 23-31. doi: 10.1097/HJR.1090b1013e32833b30932. Epub 32011 Jan 32828. **A, C**

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

(154) Varvel, S. A., Voros, S., Thiselton, D. L., Pottala, J. V., Dall, T., Warnick, G. R., McConnell, J. P., Ghaedi, L., Sasinowski, M., and Graham, T. (2014) Comprehensive biomarker testing of glycemia, insulin resistance, and beta cell function has greater sensitivity to detect diabetes risk than fasting glucose and HbA1c and is associated with improved glycemic control in clinical practice. *J Cardiovasc Transl Res.*, *7*, 597-606. doi: 510.1007/s12265-12014-19577-12261. Epub 12014 Jul 12229. **02**

(155) Xu, L., Chan, W. M., Hui, Y. F., and Lam, T. H. (2012) Association between HbA1c and cardiovascular disease mortality in older Hong Kong Chinese with diabetes. *Diabet Med.*, *29*, 393-398. doi: 310.1111/j.1464-5491.2011.03456.x. **A, C**

(156) Yang, L., Shen, X., Yan, S., Yuan, X., Lu, J., and Wei, W. (2013) HbA1c in the diagnosis of diabetes and abnormal glucose tolerance in patients with Graves' hyperthyroidism. *Diabetes Res Clin Pract.*, *101*, 28-34. doi: 10.1016/j.diabres.2013.1004.1008. Epub 2013 May 1015. **A, C**

(157) Harvey, P. W., Petkov, J., Kowanko, I., Helps, Y., and Battersby, M. (2013) Chronic condition management and self-management in Aboriginal communities in South Australia: outcomes of a longitudinal study. *Aust Health Rev.*, *37*, 246-250. doi: 210.1071/AH12165. **01**

(158) Lecube, A., Sampol, G., Munoz, X., Hernandez, C., Mesa, J., and Simo, R. (2010) Type 2 diabetes impairs pulmonary function in morbidly obese women: a case-control study. *Diabetologia.*, *53*, 1210-1216. doi: 1210.1007/s00125-00010-01700-00125. Epub 02010 Mar 00129. **R**

(159) Murphy, C. V., Coffey, R., Wisler, J., and Miller, S. F. (2013) The relationship between acute and chronic hyperglycemia and outcomes in burn injury. *J Burn Care Res.*, *34*, 109-114. doi: 110.1097/BCR.1090b1013e3182700025. **03**

(160) Wami, W. M., Buntinx, F., Bartholomeeusen, S., Goderis, G., Mathieu, C., and Aerts, M. (2013) Influence of chronic comorbidity and medication on the efficacy of treatment in patients with diabetes in general practice. *Br J Gen Pract.*, *63*, e267-273. doi: 210.3399/bjgp3313X665233. **02**

(161) Chamnan, P., Simmons, R. K., Forouhi, N. G., Luben, R. N., Khaw, K. T., Wareham, N. J., and Griffin, S. J. (2011) Incidence of type 2 diabetes using proposed HbA1c diagnostic criteria in the european prospective investigation of cancer-norfolk cohort: implications for preventive strategies. *Diabetes Care.*, *34*, 950-956. doi: 910.2337/dc2309-2326. Epub 2010 Jul 2339. **03**

(162) de Beer, J. C., and Liebenberg, L. (2014) Does cancer risk increase with HbA1c, independent of diabetes? *Br J Cancer.*, *110*, 2361-2368. doi: 2310.1038/bjc.2014.2150. Epub 2014 Mar 2327. **C**

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(163) Fowke, J. H., Matthews, C. M., Buchowski, M. S., Signorello, L. B., Chang, S. S., Cookson, M. S., and Blot, W. J. (2008) Association between prostate-specific antigen and leptin, adiponectin, HbA1c or C-peptide among African-American and Caucasian men. *Prostate Cancer Prostatic Dis*, *11*, 264-269. Epub 2007 Oct 2016. **02**

(164) Hong, S. K., Lee, S. T., Kim, S. S., Min, K. E., Byun, S. S., Cho, S. Y., Choe, G., and Lee, S. E. (2009) Significance of preoperative HbA1c level in patients with diabetes mellitus and clinically localized prostate cancer. *Prostate.*, *69*, 820-826. doi: 810.1002/pros.20932. **C**

(165) Ozbek, E., Otunctemur, A., Dursun, M., Sahin, S., Besiroglu, H., Koklu, I., Erkoc, M., Danis, E., and Bozkurt, M. (2014) Diabetes mellitus and HbA1c levels associated with high grade prostate cancer. *Asian Pac J Cancer Prev*, *15*, 2555-2558. **02**

(166) Siddiqui, A. A., Spechler, S. J., Huerta, S., Dredar, S., Little, B. B., and Cryer, B. (2008) Elevated HbA1c is an independent predictor of aggressive clinical behavior in patients with colorectal cancer: a case-control study. *Dig Dis Sci.*, *53*, 2486-2494. doi: 2410.1007/s10620-10008-10264-10624. Epub 12008 Apr 10612. **C**

(167) Sluik, D., Boeing, H., Montonen, J., Kaaks, R., Lukanova, A., Sandbaek, A., Overvad, K., Arriola, L., Ardanaz, E., Saieva, C., Grioni, S., Tumino, R., Sacerdote, C., Mattiello, A., Spijkerman, A. M., van der, A. D., Beulens, J. W., van Dieren, S., Nilsson, P. M., Groop, L. C., Franks, P. W., Rolandsson, O., Bueno-de-Mesquita, B., and Nothlings, U. (2012) HbA1c measured in stored erythrocytes is positively linearly associated with mortality in individuals with diabetes mellitus. *PLoS One*, *7*, e38877. doi: 38810.31371/journal.pone.0038877. Epub 0032012 Jun 0038813. **C**

(168) Takao, T., Matsuyama, Y., Yanagisawa, H., Kikuchi, M., and Kawazu, S. (2014) Association between HbA1c variability and mortality in patients with type 2 diabetes. *J Diabetes Complications.*, *28*, 494-499. doi: 410.1016/j.jdiacomp.2014.1002.1006. Epub 2014 Feb 1018. **C, A**

(169) Alexander, C. M., Landsman, P. B., Teutsch, S. M., and Haffner, S. M. (2003) NCEP-defined metabolic syndrome, diabetes, and prevalence of coronary heart disease among NHANES III participants age 50 years and older. *Diabetes.*, *52*, 1210-1214. **D**

(170) Anan, F., Takahashi, N., Shinohara, T., Nakagawa, M., Masaki, T., Katsuragi, I., Tanaka, K., Kakuma, T., Yonemochi, H., Eshima, N., Saikawa, T., and Yoshimatsu, H. (2006) Smoking is associated with insulin resistance and cardiovascular autonomic dysfunction in type 2 diabetic patients. *Eur J Clin Invest.*, *36*, 459-465. **D**

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(171) Baggio, B., Budakovic, A., Dalla Vestra, M., Saller, A., Bruseghin, M., and Fioretto, P. (2002) Effects of cigarette smoking on glomerular structure and function in type 2 diabetic patients. *J Am Soc Nephrol.*, *13*, 2730-2736. **D**

(172) Balkau, B., Lange, C., Fezeu, L., Tichet, J., de Lauzon-Guillain, B., Czernichow, S., Fumeron, F., Froguel, P., Vaxillaire, M., Cauchi, S., Ducimetiere, P., and Eschwege, E. (2008) Predicting diabetes: clinical, biological, and genetic approaches: data from the Epidemiological Study on the Insulin Resistance Syndrome (DESIR). *Diabetes Care.*, *31*, 2056-2061. doi: 2010.2337/dc2008-0368. Epub 2008 Aug 2058. **01**

(173) Boeing, H., Weisgerber, U. M., Jeckel, A., Rose, H. J., and Kroke, A. (2000) Association between glycated hemoglobin and diet and other lifestyle factors in a nondiabetic population: cross-sectional evaluation of data from the Potsdam cohort of the European Prospective Investigation into Cancer and Nutrition Study. *Am J Clin Nutr.*, *71*, 1115-1122. **D, F**

(174) Brewer, N., Wright, C. S., Travier, N., Cunningham, C. W., Hornell, J., Pearce, N., and Jeffreys, M. (2008) A New Zealand linkage study examining the associations between A1C concentration and mortality. *Diabetes Care.*, *31*, 1144-1149. doi: 1110.2337/dc1107-2374. Epub 2008 Feb 1125. **C**

(175) Cerami, C., Founds, H., Nicholl, I., Mitsuhashi, T., Giordano, D., Vanpatten, S., Lee, A., Al-Abed, Y., Vlassara, H., Bucala, R., and Cerami, A. (1997) Tobacco smoke is a source of toxic reactive glycation products. *Proc Natl Acad Sci U S A.*, *94*, 13915-13920. **01**

(176) Cho, N. H., Chan, J. C., Jang, H. C., Lim, S., Kim, H. L., and Choi, S. H. (2009) Cigarette smoking is an independent risk factor for type 2 diabetes: a four-year community-based prospective study. *Clin Endocrinol (Oxf).* *71*, 679-685. doi: 610.1111/j.1365-2265.2009.03586.x. Epub 02009 Mar 03528. **D**

(177) Christensen, D. L., Friis, H., Mwaniki, D. L., Kilonzo, B., Tetens, I., Boit, M. K., Omondi, B., Kaduka, L., and Borch-Johnsen, K. (2009) Prevalence of glucose intolerance and associated risk factors in rural and urban populations of different ethnic groups in Kenya. *Diabetes Res Clin Pract.*, *84*, 303-310. doi: 310.1016/j.diabres.2009.1003.1007. Epub 2009 Apr 1019. **01**

(178) Clair, C., Bitton, A., Meigs, J. B., and Rigotti, N. A. (2011) Relationships of cotinine and self-reported cigarette smoking with hemoglobin A1c in the U.S.: results from the National Health and Nutrition Examination Survey, 1999-2008. *Diabetes Care.*, *34*, 2250-2255. doi: 2210.2337/dc2211-0710. Epub 2011 Aug 2211. **D, E, F**

(179) Colagiuri, S., Colagiuri, R., Na'ati, S., Muimuiheata, S., Hussain, Z., and Palu, T. (2002) The prevalence of diabetes in the kingdom of Tonga. *Diabetes Care.*, *25*, 1378-1383. **03**

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

(180) de Vegt, F., Dekker, J. M., Ruhe, H. G., Stehouwer, C. D., Nijpels, G., Bouter, L. M., and Heine, R. J. (1999) Hyperglycaemia is associated with all-cause and cardiovascular mortality in the Hoorn population: the Hoorn Study. *Diabetologia.*, *42*, 926-931. **C**

(181) Deepa, M., Pradeepa, R., Rema, M., Mohan, A., Deepa, R., Shanthirani, S., and Mohan, V. (2003) The Chennai Urban Rural Epidemiology Study (CURES)--study design and methodology (urban component) (CURES-I). *J Assoc Physicians India.*, *51*, 863-870. **D**

(182) den Engelsen, C., van den Donk, M., Gorter, K. J., Salome, P. L., and Rutten, G. E. (2012) Advanced glycation end products measured by skin autofluorescence in a population with central obesity. *Dermatoendocrinol.*, *4*, 33-38. doi: 10.4161/derm.17999. **03**

(183) Dunstan, D. W., Zimmet, P. Z., Welborn, T. A., Cameron, A. J., Shaw, J., de Courten, M., Jolley, D., and McCarty, D. J. (2002) The Australian Diabetes, Obesity and Lifestyle Study (AusDiab)--methods and response rates. *Diabetes Res Clin Pract.*, *57*, 119-129. **D**

(184) Fujimoto, W. Y., Leonetti, D. L., Kinyoun, J. L., Newell-Morris, L., Shuman, W. P., Stolov, W. C., and Wahl, P. W. (1987) Prevalence of diabetes mellitus and impaired glucose tolerance among second-generation Japanese-American men. *Diabetes.*, *36*, 721-729. **D**

(185) Gerstein, H. C., Swedberg, K., Carlsson, J., McMurray, J. J., Michelson, E. L., Olofsson, B., Pfeffer, M. A., and Yusuf, S. (2008) The hemoglobin A1c level as a progressive risk factor for cardiovascular death, hospitalization for heart failure, or death in patients with chronic heart failure: an analysis of the Candesartan in Heart failure: Assessment of Reduction in Mortality and Morbidity (CHARM) program. *Arch Intern Med.*, *168*, 1699-1704. doi: 1610.1001/archinte.1168.1615.1699. **D, A**

(186) Gimeno, S. G., Ferreira, S. R., Franco, L. J., Hirai, A. T., Matsumura, L., and Moises, R. S. (2002) Prevalence and 7-year incidence of Type II diabetes mellitus in a Japanese-Brazilian population: an alarming public health problem. *Diabetologia.*, *45*, 1635-1638. Epub 2002 Oct 1624. **A**

(187) Glumer, C., Jorgensen, T., and Borch-Johnsen, K. (2003) Prevalences of diabetes and impaired glucose regulation in a Danish population: the Inter99 study. *Diabetes Care.*, *26*, 2335-2340. **D**

(188) Gulliford, M. C., and Ukoumunne, O. C. (2001) Determinants of glycated haemoglobin in the general population: associations with diet, alcohol and cigarette smoking. *Eur J Clin Nutr.*, *55*, 615-623. **D, E, F**

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

(189) Herman, W. H., Ali, M. A., Aubert, R. E., Engelgau, M. M., Kenny, S. J., Gunter, E. W., Malarcher, A. M., Brechner, R. J., Wetterhall, S. F., DeStefano, F., and et al. (1995) Diabetes mellitus in Egypt: risk factors and prevalence. *Diabet Med.*, *12*, 1126-1131. **D**

(190) Higgins, T., Cembrowski, G., Tran, D., Lim, E., and Chan, J. (2009) Influence of variables on hemoglobin A1c values and nonheterogeneity of hemoglobin A1c reference ranges. *J Diabetes Sci Technol.*, *3*, 644-648. **D**

(191) Hokanson, J. M., Anderson, R. L., Hennrikus, D. J., Lando, H. A., and Kendall, D. M. (2006) Integrated tobacco cessation counseling in a diabetes self-management training program: a randomized trial of diabetes and reduction of tobacco. *Diabetes Educ.*, *32*, 562-570. **F**

(192) Nilsson, P. M., Gudbjornsdottir, S., Eliasson, B., and Cederholm, J. (2004) Smoking is associated with increased HbA1c values and microalbuminuria in patients with diabetes--data from the National Diabetes Register in Sweden. *Diabetes Metab.*, *30*, 261-268. **D**

(193) Nilsson, P. M., Lind, L., Pollare, T., Berne, C., and Lithell, H. O. (1995) Increased level of hemoglobin A1c, but not impaired insulin sensitivity, found in hypertensive and normotensive smokers. *Metabolism.*, *44*, 557-561. **D**

(194) Pani, L. N., Korenda, L., Meigs, J. B., Driver, C., Chamany, S., Fox, C. S., Sullivan, L., D'Agostino, R. B., and Nathan, D. M. (2008) Effect of aging on A1C levels in individuals without diabetes: evidence from the Framingham Offspring Study and the National Health and Nutrition Examination Survey 2001-2004. *Diabetes Care.*, *31*, 1991-1996. doi: 1910.2337/dc1908-0577. Epub 2008 Jul 1915. **D**

(195) Simon, D., Senan, C., Garnier, P., Saint-Paul, M., and Papoz, L. (1989) Epidemiological features of glycated haemoglobin A1c-distribution in a healthy population. The Telecom Study. *Diabetologia.*, *32*, 864-869. **D**

(196) Smith, R. J., Koenig, R. J., Binnerts, A., Soeldner, J. S., and Aoki, T. T. (1982) Regulation of hemoglobin AIc formation in human erythrocytes in vitro. Effects of physiologic factors other than glucose. *J Clin Invest.*, *69*, 1164-1168. **D**

(197) Soulimane, S., Simon, D., Shaw, J., Witte, D., Zimmet, P., Vol, S., Borch-Johnsen, K., Magliano, D., Vistisen, D., and Balkau, B. (2012) HbA1c, fasting plasma glucose and the prediction of diabetes: Inter99, AusDiab and D.E.S.I.R. *Diabetes Res Clin Pract.*, *96*, 392-399. doi: 310.1016/j.diabres.2011.1006.1003. Epub 2011 Jul 1017. **D**

(198) Stengard, J. H., Tuomilehto, J., Pekkanen, J., Kivinen, P., Kaarsalo, E., Nissinen, A., and Karvonen, M. J. (1992) Diabetes mellitus, impaired glucose tolerance and mortality among elderly men: the Finnish cohorts of the Seven Countries Study. *Diabetologia.*, *35*, 760-765. **D**

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

(199) Targher, G., Alberiche, M., Zenere, M. B., Bonadonna, R. C., Muggeo, M., and Bonora, E. (1997) Cigarette smoking and insulin resistance in patients with noninsulin-dependent diabetes mellitus. *J Clin Endocrinol Metab.*, *82*, 3619-3624. **D**

(200) Voulgari, C., Katsilambros, N., and Tentolouris, N. (2011) Smoking cessation predicts amelioration of microalbuminuria in newly diagnosed type 2 diabetes mellitus: a 1-year prospective study. *Metabolism.*, *60*, 1456-1464. doi: 1410.1016/j.metabol.2011.1402.1014. Epub 2011 Apr 1412. **D, F**

(201) Willi, C., Bodenmann, P., Ghali, W. A., Faris, P. D., and Cornuz, J. (2007) Active smoking and the risk of type 2 diabetes: a systematic review and meta-analysis. *JAMA.*, *298*, 2654-2664. **D**

(202) Yudkin, J. S., Forrest, R. D., Jackson, C. A., Ryle, A. J., Davie, S., and Gould, B. J. (1990) Unexplained variability of glycated haemoglobin in non-diabetic subjects not related to glycaemia. *Diabetologia.*, *33*, 208-215. **D**

(203) Zhou, X., Pang, Z., Gao, W., Wang, S., Zhang, L., Ning, F., Xue, B., Chen, X., and Qiao, Q. (2011) Fresh vegetable intake and prevalence of diabetes in a Chinese population in Qingdao. *Diabetes Res Clin Pract.*, *92*, 137-142. doi: 110.1016/j.diabres.2010.1012.1034. Epub 2011 Mar 1012. **D**

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

7.2 Appendix 2 Inclusion criteria A

Bott, U., Jorgens, V., Grusser, M., Bender, R., Muhlhauser, I., and Berger, M. (1994) Predictors of glycaemic control in type 1 diabetic patients after participation in an intensified treatment and teaching programme. *Diabet Med.*, *11*, 362-371. **A**

Eliasson, B. (2003) Cigarette smoking and diabetes. *Prog Cardiovasc Dis.*, *45*, 405-413. **A**

Lundman, B. M., Asplund, K., and Norberg, A. (1990) Smoking and metabolic control in patients with insulin-dependent diabetes mellitus. *J Intern Med.*, *227*, 101-106. **A**

Benhalima, K., Standl, E., and Mathieu, C. (2011) The importance of glycemic control: how low should we go with HbA1c? Start early, go safe, go low. *J Diabetes Complications.*, *25*, 202-207. doi: 210.1016/j.jdiacomp. 2010.1003.1002. Epub 2010 May 1011. **A**

Kowall, B., and Rathmann, W. (2013) HbA1c for diagnosis of type 2 diabetes. Is there an optimal cut point to assess high risk of diabetes complications, and how well does the 6.5% cutoff perform? *Diabetes Metab Syndr Obes.*, *6:477-91.*, 10.2147/DMSO.S39093. **R, A**

Kurukulasuriya, L. R., and Sowers, J. R. (2010) Therapies for type 2 diabetes: lowering HbA1c and associated cardiovascular risk factors. *Cardiovasc Diabetol.*, *9:45.*, 10.1186/1475-2840-1189-1145. **R, A**

Letourneau, J., Bui, H., Schricker, T., and Hatzakorzian, R. (2013) HbA1c: a prognostic biomarker in the surgical and critically ill patient population. *J Cardiothorac Vasc Anesth.*, *27*, 760-764. doi:710.1053/j.jvca.2012.1006.1030. Epub 2012 Aug 1031. **R, A**

Seitz, P., Rosemann, T., Gensichen, J., and Huber, C. A. (2011) Interventions in primary care to improve cardiovascular risk factors and glycated haemoglobin (HbA1c) levels in patients with diabetes: a systematic review. *Diabetes Obes Metab.*, *13*, 479-489. doi: 410.1111/j.1463-1326.2010.01347.x. **R, A**

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

Sturm, G., Lamina, C., Zitt, E., Lhotta, K., Haider, F., Neyer, U., and Kronenberg, F. (2011) Association of HbA1c values with mortality and cardiovascular events in diabetic dialysis patients. The INVOR study and review of the literature. *PLoS One*, *6*, e20093. doi: 20010.21371/journal.pone.0020093. Epub 0022011 May 0020018. **R, A, C**

ten Brinke, R., Dekker, N., de Groot, M., and Ikkersheim, D. (2008) Lowering HbA1c in type 2 diabetics results in reduced risk of coronary heart disease and all-cause mortality. *Prim Care Diabetes.*, *2*, 45-49. doi: 10.1016/j.pcd.2007.1012.1004. Epub 2008 Feb 1018. **R, A, C**

Tennyson, C., Lee, R., and Attia, R. (2013) Is there a role for HbA1c in predicting mortality and morbidity outcomes after coronary artery bypass graft surgery? *Interact Cardiovasc Thorac Surg.*, *17*, 1000-1008. doi: 1010.1093/icvts/ivt1351. Epub 2013 Sep 1010. **R, A**

Umpierre, D., Ribeiro, P. A., Kramer, C. K., Leitao, C. B., Zucatti, A. T., Azevedo, M. J., Gross, J. L., Ribeiro, J. P., and Schaan, B. D. (2011) Physical activity advice only or structured exercise training and association with HbA1c levels in type 2 diabetes: a systematic review and meta-analysis. JAMA., 305, 1790-1799. doi: 1710.1001/jama.2011.1576. **R, A, C**

Borg, R., Vistisen, D., Witte, D. R., and Borch-Johnsen, K. (2010) Comparing risk profiles of individuals diagnosed with diabetes by OGTT and HbA1c The Danish Inter99 study. *Diabet Med.*, *27*, 906-910. doi: 910.1111/j.1464-5491.2010.03034.x. **D, A**

Cederholm, J., Zethelius, B., Nilsson, P. M., Eeg-Olofsson, K., Eliasson, B., and Gudbjornsdottir, S. (2009) Effect of tight control of HbA1c and blood pressure on cardiovascular diseases in type 2 diabetes: an observational study from the Swedish National Diabetes Register (NDR). *Diabetes Res Clin Pract.*, *86*, 74-81. doi: 10.1016/j.diabres.2009.1007.1003. Epub 2009 Aug 1012. **A, D**

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

Choi, Y. J., Park, J. S., Kim, U., Lee, S. H., Son, J. W., Shin, D. G., Kim, Y. J., Jeong, M. H., Ahn, Y. K., Cho, M. C., Bae, J. W., Kim, C. J., Cho, J. M., Han, K. R., and Lee, J. H. (2013) Changes in smoking behavior and adherence to preventive guidelines among smokers after a heart attack. *J Geriatr Cardiol.*, *10*, 146-150. doi: 110.3969/j.issn.1671-5411.2013.3902.3006. **F, A**

Diez-Espino, J., Buil-Cosiales, P., Serrano-Martinez, M., Toledo, E., Salas-Salvado, J., and Martinez-Gonzalez, M. A. (2011) Adherence to the Mediterranean diet in patients with type 2 diabetes mellitus and HbA1c level. *Ann Nutr Metab*, *58*, 74-78. doi: 10.1159/000324718. Epub 000322011 Mar 000324724. **D, A**

Hayashida, H., Kawasaki, K., Yoshimura, A., Kitamura, M., Furugen, R., Nakazato, M., Takamura, N., Hara, Y., Maeda, T., and Saito, T. (2009) Relationship between periodontal status and HbA1c in nondiabetics. *J Public Health Dent.*, *69*, 204-206. doi: 210.1111/j.1752-7325.2009.00122.x. **A, D**

Jansen, H., Stolk, R. P., Nolte, I. M., Kema, I. P., Wolffenbuttel, B. H., and Snieder, H. (2013) Determinants of HbA1c in nondiabetic Dutch adults: genetic loci and clinical and lifestyle parameters, and their interactions in the Lifelines Cohort Study. *J Intern Med.*, *273*, 283-293. doi: 210.1111/joim.12010. Epub 12012 Dec 12015. **A, D**

M, M., Sembian, U., Babitha, N, E., and K, M. (2014) Study of Auditory, Visual Reaction Time and Glycemic Control (HBA1C) in Chronic Type II Diabetes Mellitus. *J Clin Diagn Res.*, *8*, BC11-13. doi: 10.7860/JCDR/2014/8906.4865. Epub 2014 Sep 7820. **A**

Power, C., Atherton, K., and Thomas, C. (2010) Maternal smoking in pregnancy, adult adiposity and other risk factors for cardiovascular disease. Atherosclerosis., 211, 643-648. doi: 610.1016/j.atherosclerosis.2010.1003.1015. Epub 2010 Mar 1016. **D, A**

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

Qie, L. Y., Sun, J. P., Ning, F., Pang, Z. C., Gao, W. G., Ren, J., Nan, H. R., Zhang, L., and Qiao, Q. (2014) Cardiovascular risk profiles in relation to newly diagnosed type 2 diabetes diagnosed by either glucose or HbA1c criteria in Chinese adults in Qingdao, China. *Diabet Med.*, *31*, 920-926. doi: 910.1111/dme.12498. Epub 12014 Jun 12492. **A, D**

Schwab, K. O., Doerfer, J., Hallermann, K., Krebs, A., Schorb, E., Krebs, K., and Winkler, K. (2008) Marked smoking-associated increase of cardiovascular risk in childhood type 1 diabetes. Int J Adolesc Med Health., 20, 285-292. **A, D**

Suchitra, M. R., Jaiganesh, K., and Parthasarathy, S. (2013) Diabetic Profile- Screening of HBA1C - A Random Community Assessment. *J Clin Diagn Res.*, *7*, 2200-2202. doi: 2210.7860/JCDR/2013/5690.3470. Epub 2013 Oct 2205. **D, A**

Uruska, A., Araszkiewicz, A., Uruski, P., and Zozulinska-Ziolkiewicz, D. (2014) Higher risk of microvascular complications in smokers with type 1 diabetes despite intensive insulin therapy. Microvasc Res., 92:79-84., 10.1016/j.mvr.2014.1001.1002. Epub 2014 Jan 1012. **D, A**

Wang, C., Song, J., Ma, Z., Yang, W., Li, C., Zhang, X., Hou, X., Sun, Y., Lin, P., Liang, K., Gong, L., Wang, M., Liu, F., Li, W., Yan, F., Yang, J., Wang, L., Tian, M., Liu, J., Zhao, R., and Chen, L. (2014) Fluctuation between fasting and 2-H postload glucose state is associated with chronic kidney disease in previously diagnosed type 2 diabetes patients with HbA1c >/= 7%. *PLoS One.*, *9*, e102941. doi: 102910.101371/journal.pone.0102941. eCollection 0102014. **A, C**

Zhao, W., Katzmarzyk, P. T., Horswell, R., Wang, Y., Johnson, J., Heymsfield, S. B., Cefalu, W. T., Ryan, D. H., and Hu, G. (2013) HbA1c and lower-extremity amputation risk in low-income patients with diabetes. *Diabetes Care.*, *36*, 3591-3598. doi: 3510.2337/dc3513-0437. Epub 2013 Sep 3523. **A, C**

Zhao, W., Katzmarzyk, P. T., Horswell, R., Wang, Y., Johnson, J., and Hu, G. (2014) HbA1c and heart failure risk among diabetic patients. *J Clin Endocrinol Metab.*, *99*, E263-267. doi: 210.1210/jc.2013-3325. Epub 2013 Jan 1211. **D, A**

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

Zhao, W., Katzmarzyk, P. T., Horswell, R., Wang, Y., Johnson, J., and Hu, G. (2014) HbA1c and coronary heart disease risk among diabetic patients. *Diabetes Care.*, *37*, 428-435. doi: 410.2337/dc2313-1525. Epub 2013 Oct 2315. **D, A**

Andersson, C., van Gaal, L., Caterson, I. D., Weeke, P., James, W. P., Coutinho, W., Finer, N., Sharma, A. M., Maggioni, A. P., and Torp-Pedersen, C. (2012) Relationship between HbA1c levels and risk of cardiovascular adverse outcomes and all-cause mortality in overweight and obese cardiovascular high-risk women and men with type 2 diabetes. *Diabetologia.*, *55*, 2348-2355. doi: 2310.1007/s00125-00012-02584-00123. Epub 02012 May 00126. **A, C**

Bouchi, R., Babazono, T., Mugishima, M., Yoshida, N., Nyumura, I., Toya, K., Hayashi, T., Hanai, K., Tanaka, N., Ishii, A., and Iwamoto, Y. (2012) Fluctuations in HbA1c are associated with a higher incidence of cardiovascular disease in Japanese patients with type 2 diabetes. *J Diabetes Investig.*, *3*, 148-155. doi: 110.1111/j.2040-1124.2011.00155.x. **A**

Chamnan, P., Simmons, R. K., Khaw, K. T., Wareham, N. J., and Griffin, S. J. (2013) Change in HbA1c over 3 years does not improve the prediction of cardiovascular disease over and above HbA1c measured at a single time point. Diabetologia., 56, 1004-1011. doi: 1010.1007/s00125-00013-02854-00128. Epub 02013 Feb 00112. **A**

Eeg-Olofsson, K., Cederholm, J., Nilsson, P. M., Zethelius, B., Svensson, A. M., Gudbjornsdottir, S., and Eliasson, B. (2010) New aspects of HbA1c as a risk factor for cardiovascular diseases in type 2 diabetes: an observational study from the Swedish National Diabetes Register (NDR). *J Intern Med.*, *268*, 471-482. doi: 410.1111/j.1365-2796.2010.02265.x. **A, C**

Gao, L., Matthews, F. E., Sargeant, L. A., and Brayne, C. (2008) An investigation of the population impact of variation in HbA1c levels in older people in England and Wales: from a population based multi-centre longitudinal study. *BMC Public Health.*, *8:54.*, 10.1186/1471-2458-1188-1154. **A, C**

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

Hernandez, D., Espejo-Gil, A., Bernal-Lopez, M. R., Mancera-Romero, J., Baca-Osorio, A. J., Tinahones, F. J., Armas-Padron, A. M., Ruiz-Esteban, P., Torres, A., and Gomez-Huelgas, R. (2013) Association of HbA1c and cardiovascular and renal disease in an adult Mediterranean population. *BMC Nephrol.*, *14:151.*, 10.1186/1471-2369-1114-1151. **A, C**

K, P., Kunikullaya, U. K., and Goturu, J. (2014) Glycosylated Haemoglobin (HbA1c) - A Marker of Circulating Lipids in Type 2 Diabetic Patients. *J Clin Diagn Res.*, *8*, 20-23. doi: 10.7860/JCDR/2014/7742.3996. Epub 2014 Feb 7863. **A**

Khaw, K. T. (2009) Elevated HbA1c level: a risk factor for cardiovascular disease mortality in patients with chronic heart failure? *Nat Clin Pract Endocrinol Metab.*, *5*, 130-131. doi: 110.1038/ncpendmet1069. **A**

Kilpatrick, E. S., Rigby, A. S., and Atkin, S. L. (2008) Mean blood glucose compared with HbA1c in the prediction of cardiovascular disease in patients with type 1 diabetes. *Diabetologia.*, *51*, 365-371. Epub 2007 Nov 2027. **A**

Luk, A. O., Ma, R. C., Lau, E. S., Yang, X., Lau, W. W., Yu, L. W., Chow, F. C., Chan, J. C., and So, W. Y. (2013) Risk association of HbA1c variability with chronic kidney disease and cardiovascular disease in type 2 diabetes: prospective analysis of the Hong Kong Diabetes Registry. *Diabetes Metab Res Rev.*, *29*, 384-390. doi: 310.1002/dmrr.2404. **A, C**

Nathan, D. M., McGee, P., Steffes, M. W., and Lachin, J. M. (2014) Relationship of glycated albumin to blood glucose and HbA1c values and to retinopathy, nephropathy, and cardiovascular outcomes in the DCCT/EDIC study. *Diabetes.*, *63*, 282-290. doi: 210.2337/db2313-0782. Epub 2013 Aug 2329. **A**

van 't Riet, E., Rijkelijkhuizen, J. M., Alssema, M., Nijpels, G., Ste **A** houwer, C. D., Heine, R. J., and Dekker, J. M. (2012) HbA1c is an independent predictor of non-fatal cardiovascular disease in a Caucasian population without diabetes: a 10-year follow-up of the Hoorn Study. *Eur J Prev Cardiol.*, *19*, 23-31. doi: 10.1097/HJR.1090b1013e32833b30932. Epub 32011 Jan 32828. **A, C**

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

Yang, L., Shen, X., Yan, S., Yuan, X., Lu, J., and Wei, W. (2013) HbA1c in the diagnosis of diabetes and abnormal glucose tolerance in patients with Graves' hyperthyroidism. *Diabetes Res Clin Pract.*, *101*, 28-34. doi: 10.1016/j.diabres.2013.1004.1008. Epub 2013 May 1015. **A, C**

Takao, T., Matsuyama, Y., Yanagisawa, H., Kikuchi, M., and Kawazu, S. (2014) Association between HbA1c variability and mortality in patients with type 2 diabetes. *J Diabetes Complications.*, *28*, 494-499. doi: 410.1016/j.jdiacomp.2014.1002.1006. Epub 2014 Feb 1018. **C, A**

Gerstein, H. C., Swedberg, K., Carlsson, J., McMurray, J. J., Michelson, E. L., Olofsson, B., Pfeffer, M. A., and Yusuf, S. (2008) The hemoglobin A1c level as a progressive risk factor for cardiovascular death, hospitalization for heart failure, or death in patients with chronic heart failure: an analysis of the Candesartan in Heart failure: Assessment of Reduction in Mortality and Morbidity (CHARM) program. Arch Intern Med., 168, 1699-1704. doi: 1610.1001/archinte.1168.1615.1699. **D, A**

Gimeno, S. G., Ferreira, S. R., Franco, L. J., Hirai, A. T., Matsumura, L., and Moises, R. S. (2002) Prevalence and 7-year incidence of Type II diabetes mellitus in a Japanese-Brazilian population: an alarming public health problem. *Diabetologia.*, *45*, 1635-1638. Epub 2002 Oct 1624. **A**

Pacilli, A., De Cosmo, S., Trischitta, V., and Bacci, S. (2013) Role of relationship between HbA1c, fibrinogen and HDL-cholesterol on cardiovascular disease in patients with type 2 diabetes mellitus. *Atherosclerosis.*, *228*, 247-248. doi: 210.1016/j.atherosclerosis.2013.1002.1010. Epub 2013 Feb 1020. **A**

Xu, L., Chan, W. M., Hui, Y. F., and Lam, T. H. (2012) Association between HbA1c and cardiovascular disease mortality in older Hong Kong Chinese with diabetes. *Diabet Med.*, *29*, 393-398. doi: 310.1111/j.1464-5491.2011.03456.x. **A, C**

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

7.3 Appendix 3 Inclusion criteria B

None

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7.4 Appendix 4 Inclusion criteria C

Liew, A. K., Punnanithinont, N., Lee, Y. C., and Yang, J. (2013) Effect of non-surgical periodontal treatment on HbA1c: a meta-analysis of randomized controlled trials. *Aust Dent J.*, *58*, 350-357. doi: 310.1111/adj.12091. **R, C**

Rollins, K. E., Varadhan, K. K., Dhatariya, K., and Lobo, D. N. (2015) Systematic review of the impact of HbA1c on outcomes following surgery in patients with diabetes mellitus. *Clin Nutr*, *17*, 00082-00085. **R, C**

Sturm, G., Lamina, C., Zitt, E., Lhotta, K., Haider, F., Neyer, U., and Kronenberg, F. (2011) Association of HbA1c values with mortality and cardiovascular events in diabetic dialysis patients. The INVOR study and review of the literature. *PLoS One*, *6*, e20093. doi: 20010.21371/journal.pone.0020093. Epub 0022011 May 0020018. **R, A, C**

ten Brinke, R., Dekker, N., de Groot, M., and Ikkersheim, D. (2008) Lowering HbA1c in type 2 diabetics results in reduced risk of coronary heart disease and all-cause mortality. *Prim Care Diabetes.*, *2*, 45-49. doi: 10.1016/j.pcd.2007.1012.1004. Epub 2008 Feb 1018. **R, A, C**

Umpierre, D., Ribeiro, P. A., Kramer, C. K., Leitao, C. B., Zucatti, A. T., Azevedo, M. J., Gross, J. L., Ribeiro, J. P., and Schaan, B. D. (2011) Physical activity advice only or structured exercise training and association with HbA1c levels in type 2 diabetes: a systematic review and meta-analysis. *JAMA.*, *305*, 1790-1799. doi: 1710.1001/jama.2011.1576. **R, A, C**

Aggarwal, J., and Kumar, M. (2014) Prevalence of Microalbuminuria among Rural North Indian Population with Diabetes Mellitus and its Correlation with Glycosylated Haemoglobin and Smoking. *J Clin Diagn Res.*, *8*, CC11-13. doi: 10.7860/JCDR/2014/9758.4613. Epub 2014 Jul 7820. **C**

Fan, Y., Huang, X. D., Zhang, H., Wu, J., Zhang, X. X., and Luo, H. S. (2014) Association between serum HbA1c levels and adenomatous polyps in patients with the type 2 diabetes mellitus. *Minerva Endocrinol*, *8*, 8. **C**

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

Herbert, M. S., Varley, A. L., Andreae, S. J., Goodin, B. R., Bradley, L. A., and Safford, M. M. (2013) Association of pain with HbA1c in a predominantly black population of community-dwelling adults with diabetes: a cross-sectional analysis. *Diabet Med.*, *30*, 1466-1471. doi: 1410.1111/dme.12264. Epub 12013 Jul 12219. **C**

Hodge, P. J., Robertson, D., Paterson, K., Smith, G. L., Creanor, S., and Sherriff, A. (2012) Periodontitis in non-smoking type 1 diabetic adults: a cross-sectional study. *J Clin Periodontol.*, *39*, 20-29. doi: 10.1111/j.1600-1051X.2011.01791.x. Epub 02011 Oct 01731. **C**

Hou, R. L., Zhou, H. H., Chen, X. Y., Wang, X. M., Shao, J., and Zhao, Z. Y. (2014) Effect of maternal lipid profile, C-peptide, insulin, and HBA1c levels during late pregnancy on large-for-gestational age newborns. *World J Pediatr.*, *10*, 175-181. doi: 110.1007/s12519-12014-10488-12517. Epub 12014 May 12517. **C**

Kerr, D., Partridge, H., Knott, J., and Thomas, P. W. (2011) HbA1c 3 months after diagnosis predicts premature mortality in patients with new onset type 2 diabetes. Diabet Med., 28, 1520-1524. doi: 1510.1111/j.1464-5491.2011.03443.x. **D, C**

Levitan, E. B., Liu, S., Stampfer, M. J., Cook, N. R., Rexrode, K. M., Ridker, P. M., Buring, J. E., and Manson, J. E. (2008) HbA1c measured in stored erythrocytes and mortality rate among middle-aged and older women. *Diabetologia.*, *51*, 267-275. Epub 2007 Nov 2028. **C**

Melin, E. O., Thunander, M., Landin-Olsson, M., Hillman, M., and Thulesius, H. O. (2014) Depression, smoking, physical inactivity and season independently associated with midnight salivary cortisol in type 1 diabetes. *BMC Endocr Disord.*, *14:75.*, 10.1186/1472-6823-1114-1175. **C**

Melin, E. O., Thunander, M., Svensson, R., Landin-Olsson, M., and Thulesius, H. O. (2013) Depression, obesity, and smoking were independently associated with inadequate glycemic control in patients with type 1 diabetes. Eur J Endocrinol., 168, 861-869. doi: 810.1530/EJE-1513-0137. Print 2013 Jun. **D, C**

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

Miao Jonasson, J., Cederholm, J., Eliasson, B., Zethelius, B., Eeg-Olofsson, K., and Gudbjornsdottir, S. (2012) HbA1C and cancer risk in patients with type 2 diabetes--a nationwide population-based prospective cohort study in Sweden. PLoS One, 7, e38784. doi: 38710.31371/journal.pone.0038784. Epub 0032012 Jun 0038714. **C**

No, J. I., Yang, J. Y., Hyun, H. J., Yeon, C. S., and Choi, H. J. (2013) Factors Associated with Serum Levels of Carcinoembryonic Antigen in Healthy Non-smokers. *Korean J Fam Med.*, *34*, 413-419. doi: 410.4082/kjfm.2013.4034.4086.4413. Epub 2013 Nov 4025. **C**

Sanz, C. M., Ruidavets, J. B., Bongard, V., Marquie, J. C., Hanaire, H., Ferrieres, J., and Andrieu, S. (2013) Relationship between markers of insulin resistance, markers of adiposity, HbA1c, and cognitive functions in a middle-aged population-based sample: the MONA LISA study. Diabetes Care., 36, 1512-1521. doi: 1510.2337/dc1512-1017. Epub 2012 Dec 1528. **D, C**

Susanto, H., Nesse, W., Dijkstra, P. U., Hoedemaker, E., van Reenen, Y. H., Agustina, D., Vissink, A., and Abbas, F. (2012) Periodontal inflamed surface area and C-reactive protein as predictors of HbA1c: a study in Indonesia. *Clin Oral Investig.*, *16*, 1237-1242. doi: 1210.1007/s00784-00011-00621-00780. Epub 02011 Oct 00720. **D, C**

Wang, C., Song, J., Ma, Z., Yang, W., Li, C., Zhang, X., Hou, X., Sun, Y., Lin, P., Liang, K., Gong, L., Wang, M., Liu, F., Li, W., Yan, F., Yang, J., Wang, L., Tian, M., Liu, J., Zhao, R., and Chen, L. (2014) Fluctuation between fasting and 2-H postload glucose state is associated with chronic kidney disease in previously diagnosed type 2 diabetes patients with HbA1c >/= 7%. *PLoS One.*, *9*, e102941. doi: 102910.101371/journal.pone.0102941. eCollection 0102014. **A, C**

Zhao, W., Katzmarzyk, P. T., Horswell, R., Wang, Y., Johnson, J., Heymsfield, S. B., Cefalu, W. T., Ryan, D. H., and Hu, G. (2013) HbA1c and lower-extremity amputation risk in low-income patients with diabetes. *Diabetes Care.*, *36*, 3591-3598. doi: 3510.2337/dc3513-0437. Epub 2013 Sep 3523. **A, C**

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

Andersson, C., van Gaal, L., Caterson, I. D., Weeke, P., James, W. P., Coutinho, W., Finer, N., Sharma, A. M., Maggioni, A. P., and Torp-Pedersen, C. (2012) Relationship between HbA1c levels and risk of cardiovascular adverse outcomes and all-cause mortality in overweight and obese cardiovascular high-risk women and men with type 2 diabetes. *Diabetologia.*, *55*, 2348-2355. doi: 2310.1007/s00125-00012-02584-00123. Epub 02012 May 00126. **A, C**

Eeg-Olofsson, K., Cederholm, J., Nilsson, P. M., Zethelius, B., Svensson, A. M., Gudbjornsdottir, S., and Eliasson, B. (2010) New aspects of HbA1c as a risk factor for cardiovascular diseases in type 2 diabetes: an observational study from the Swedish National Diabetes Register (NDR). *J Intern Med.*, *268*, 471-482. doi: 410.1111/j.1365-2796.2010.02265.x. **A, C**

Gao, L., Matthews, F. E., Sargeant, L. A., and Brayne, C. (2008) An investigation of the population impact of variation in HbA1c levels in older people in England and Wales: from a population based multi-centre longitudinal study. *BMC Public Health.*, *8:54.*, 10.1186/1471-2458-1188-1154. **A, C**

Hernandez, D., Espejo-Gil, A., Bernal-Lopez, M. R., Mancera-Romero, J., Baca-Osorio, A. J., Tinahones, F. J., Armas-Padron, A. M., Ruiz-Esteban, P., Torres, A., and Gomez-Huelgas, R. (2013) Association of HbA1c and cardiovascular and renal disease in an adult Mediterranean population. *BMC Nephrol.*, *14:151.*, 10.1186/1471-2369-1114-1151. **A, C**

Lerstad, G., Brodin, E. E., Enga, K. F., Jorde, R., Schirmer, H., Njolstad, I., Svartberg, J., Braekkan, S. K., and Hansen, J. B. (2014) Hyperglycemia, assessed according to HbA1c , and future risk of venous thromboembolism: the Tromso study. *J Thromb Haemost*, *12*, 313-319. doi: 310.1111/jth.12498. **C**

Luk, A. O., Ma, R. C., Lau, E. S., Yang, X., Lau, W. W., Yu, L. W., Chow, F. C., Chan, J. C., and So, W. Y. (2013) Risk association of HbA1c variability with chronic kidney disease and cardiovascular disease in type 2 diabetes: prospective analysis of the Hong

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

Kong Diabetes Registry. *Diabetes Metab Res Rev.*, *29*, 384-390. doi: 310.1002/dmrr.2404. **A, C**

van 't Riet, E., Rijkelijkhuizen, J. M., Alssema, M., Nijpels, G., Ste **A** houwer, C. D., Heine, R. J., and Dekker, J. M. (2012) HbA1c is an independent predictor of non-fatal cardiovascular disease in a Caucasian population without diabetes: a 10-year follow-up of the Hoorn Study. *Eur J Prev Cardiol.*, *19*, 23-31. doi: 10.1097/HJR.1090b1013e32833b30932. Epub 32011 Jan 32828. **A, C**

Yang, L., Shen, X., Yan, S., Yuan, X., Lu, J., and Wei, W. (2013) HbA1c in the diagnosis of diabetes and abnormal glucose tolerance in patients with Graves' hyperthyroidism. *Diabetes Res Clin Pract.*, *101*, 28-34. doi: 10.1016/j.diabres.2013.1004.1008. Epub 2013 May 1015. **A, C**

de Beer, J. C., and Liebenberg, L. (2014) Does cancer risk increase with HbA1c, independent of diabetes? *Br J Cancer.*, *110*, 2361-2368. doi: 2310.1038/bjc.2014.2150. Epub 2014 Mar 2327. **C**

Hong, S. K., Lee, S. T., Kim, S. S., Min, K. E., Byun, S. S., Cho, S. Y., Choe, G., and Lee, S. E. (2009) Significance of preoperative HbA1c level in patients with diabetes mellitus and clinically localized prostate cancer. *Prostate.*, *69*, 820-826. doi: 810.1002/pros.20932. **C**

Siddiqui, A. A., Spechler, S. J., Huerta, S., Dredar, S., Little, B. B., and Cryer, B. (2008) Elevated HbA1c is an independent predictor of aggressive clinical behavior in patients with colorectal cancer: a case-control study. *Dig Dis Sci.*, *53*, 2486-2494. doi: 2410.1007/s10620-10008-10264-10624. Epub 12008 Apr 10612. **C**

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

Sluik, D., Boeing, H., Montonen, J., Kaaks, R., Lukanova, A., Sandbaek, A., Overvad, K., Arriola, L., Ardanaz, E., Saieva, C., Grioni, S., Tumino, R., Sacerdote, C., Mattiello, A., Spijkerman, A. M., van der, A. D., Beulens, J. W., van Dieren, S., Nilsson, P. M., Groop, L. C., Franks, P. W., Rolandsson, O., Bueno-de-Mesquita, B., and Nothlings, U. (2012) HbA1c measured in stored erythrocytes is positively linearly associated with mortality in individuals with diabetes mellitus. *PLoS One*, *7*, e38877. doi: 38810.31371/journal.pone.0038877. Epub 0032012 Jun 0038813. **C**

Takao, T., Matsuyama, Y., Yanagisawa, H., Kikuchi, M., and Kawazu, S. (2014) Association between HbA1c variability and mortality in patients with type 2 diabetes. *J Diabetes Complications.*, *28*, 494-499. doi: 410.1016/j.jdiacomp.2014.1002.1006. Epub 2014 Feb 1018. **C, A**

Brewer, N., Wright, C. S., Travier, N., Cunningham, C. W., Hornell, J., Pearce, N., and Jeffreys, M. (2008) A New Zealand linkage study examining the associations between A1C concentration and mortality. Diabetes Care., 31, 1144-1149. doi: 1110.2337/dc1107-2374. Epub 2008 Feb 1125. **C**

de Vegt, F., Dekker, J. M., Ruhe, H. G., Stehouwer, C. D., Nijpels, G., Bouter, L. M., and Heine, R. J. (1999) Hyperglycaemia is associated with all-cause and cardiovascular mortality in the Hoorn population: the Hoorn Study. *Diabetologia.*, *42*, 926-931. **C**

Xu, L., Chan, W. M., Hui, Y. F., and Lam, T. H. (2012) Association between HbA1c and cardiovascular disease mortality in older Hong Kong Chinese with diabetes. *Diabet Med.*, *29*, 393-398. doi: 310.1111/j.1464-5491.2011.03456.x. **A, C**

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

7.5 Appendix 5 Inclusion criteria D

Sargeant, L. A., Khaw, K. T., Bingham, S., Day, N. E., Luben, R. N., Oakes, S., Welch, A., and Wareham, N. J. (2001) Cigarette smoking and glycaemia: the EPIC-Norfolk Study. European Prospective Investigation into Cancer. *Int J Epidemiol.*, *30*, 547-554. **D**

Borg, R., Vistisen, D., Witte, D. R., and Borch-Johnsen, K. (2010) Comparing risk profiles of individuals diagnosed with diabetes by OGTT and HbA1c The Danish Inter99 study. *Diabet Med.*, *27*, 906-910. doi: 910.1111/j.1464-5491.2010.03034.x. **D, A**

Cederholm, J., Zethelius, B., Nilsson, P. M., Eeg-Olofsson, K., Eliasson, B., and Gudbjornsdottir, S. (2009) Effect of tight control of HbA1c and blood pressure on cardiovascular diseases in type 2 diabetes: an observational study from the Swedish National Diabetes Register (NDR). *Diabetes Res Clin Pract.*, *86*, 74-81. doi: 10.1016/j.diabres.2009.1007.1003. Epub 2009 Aug 1012. **A, D**

Diez-Espino, J., Buil-Cosiales, P., Serrano-Martinez, M., Toledo, E., Salas-Salvado, J., and Martinez-Gonzalez, M. A. (2011) Adherence to the Mediterranean diet in patients with type 2 diabetes mellitus and HbA1c level. *Ann Nutr Metab*, *58*, 74-78. doi: 10.1159/000324718. Epub 000322011 Mar 000324724. **D, A**

Gerber, P. A., Locher, R., Schmid, B., Spinas, G. A., and Lehmann, R. (2013) Smoking is associated with impaired long-term glucose metabolism in patients with type 1 diabetes mellitus. *Nutr Metab Cardiovasc Dis.*, *23*, 102-108. doi: 110.1016/j.numecd.2011.1008.1007. Epub 2011 Nov 1025. **D**

Hayashida, H., Kawasaki, K., Yoshimura, A., Kitamura, M., Furugen, R., Nakazato, M., Takamura, N., Hara, Y., Maeda, T., and Saito, T. (2009) Relationship between periodontal status and HbA1c in nondiabetics. *J Public Health Dent.*, *69*, 204-206. doi: 210.1111/j.1752-7325.2009.00122.x. **A, D**

Hofer, S. E., Rosenbauer, J., Grulich-Henn, J., Naeke, A., Frohlich-Reiterer, E., and Holl, R. W. (2009) Smoking and metabolic control in adolescents with type 1 diabetes. *J Pediatr.*, *154*, 20-23.e21. doi: 10.1016/j.jpeds.2008.1007.1052. Epub 2008 Sep 1019. **D**

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

Jansen, H., Stolk, R. P., Nolte, I. M., Kema, I. P., Wolffenbuttel, B. H., and Snieder, H. (2013) Determinants of HbA1c in nondiabetic Dutch adults: genetic loci and clinical and lifestyle parameters, and their interactions in the Lifelines Cohort Study. *J Intern Med.*, *273*, 283-293. doi: 210.1111/joim.12010. Epub 12012 Dec 12015. **A, D**

Kerr, D., Partridge, H., Knott, J., and Thomas, P. W. (2011) HbA1c 3 months after diagnosis predicts premature mortality in patients with new onset type 2 diabetes. Diabet Med., 28, 1520-1524. doi: 1510.1111/j.1464-5491.2011.03443.x. **D, C**

Kotani, K., Sakane, N., Miyamoto, M., Yamada, K., and Taniguchi, N. (2010) Influence of smoking habits on the GA/HbA1c ratio in patients with type 1 diabetes mellitus. *Med Princ Pract*, *19*, 415-417. doi: 410.1159/000316385. Epub 000312010 Jul 000316314. **D**

Melin, E. O., Thunander, M., Svensson, R., Landin-Olsson, M., and Thulesius, H. O. (2013) Depression, obesity, and smoking were independently associated with inadequate glycemic control in patients with type 1 diabetes. Eur J Endocrinol., 168, 861-869. doi: 810.1530/EJE-1513-0137. Print 2013 Jun. **D, C**

Ohkuma, T., Iwase, M., Fujii, H., Kaizu, S., Ide, H., Jodai, T., Kikuchi, Y., Idewaki, Y., Hirakawa, Y., Nakamura, U., and Kitazono, T. (2015) Dose- and time-dependent association of smoking and its cessation with glycemic control and insulin resistance in male patients with type 2 diabetes mellitus: the fukuoka diabetes registry. *PLoS One.*, *10*, e0122023. doi: 0122010.0121371/journal.pone.0122023. eCollection 0122015. **D, E, F**

Power, C., Atherton, K., and Thomas, C. (2010) Maternal smoking in pregnancy, adult adiposity and other risk factors for cardiovascular disease. Atherosclerosis., 211, 643-648. doi: 610.1016/j.atherosclerosis.2010.1003.1015. Epub 2010 Mar 1016. **D, A**

Qie, L. Y., Sun, J. P., Ning, F., Pang, Z. C., Gao, W. G., Ren, J., Nan, H. R., Zhang, L., and Qiao, Q. (2014) Cardiovascular risk profiles in relation to newly diagnosed type 2 diabetes diagnosed by either glucose or HbA1c criteria in Chinese adults in Qingdao, China. *Diabet Med.*, *31*, 920-926. doi: 910.1111/dme.12498. Epub 12014 Jun 12492. **A, D**

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

Sanz, C. M., Ruidavets, J. B., Bongard, V., Marquie, J. C., Hanaire, H., Ferrieres, J., and Andrieu, S. (2013) Relationship between markers of insulin resistance, markers of adiposity, HbA1c, and cognitive functions in a middle-aged population-based sample: the MONA LISA study. Diabetes Care., 36, 1512-1521. doi: 1510.2337/dc1512-1017. Epub 2012 Dec 1528. **D, C**

Schwab, K. O., Doerfer, J., Hallermann, K., Krebs, A., Schorb, E., Krebs, K., and Winkler, K. (2008) Marked smoking-associated increase of cardiovascular risk in childhood type 1 diabetes. Int J Adolesc Med Health., 20, 285-292. **A, D**

Soulimane, S., Simon, D., Herman, W. H., Lange, C., Lee, C. M., Colagiuri, S., Shaw, J. E., Zimmet, P. Z., Magliano, D., Ferreira, S. R., Dong, Y., Zhang, L., Jorgensen, T., Tuomilehto, J., Mohan, V., Christensen, D. L., Kaduka, L., Dekker, J. M., Nijpels, G., Stehouwer, C. D., Lantieri, O., Fujimoto, W. Y., Leonetti, D. L., McNeely, M. J., Borch-Johnsen, K., Boyko, E. J., Vistisen, D., and Balkau, B. (2014) HbA1c, fasting and 2 h plasma glucose in current, ex- and never-smokers: a meta-analysis. *Diabetologia.*, *57*, 30-39. doi: 10.1007/s00125-00013-03058-y. Epub 02013 Sep 00125. **D**

Suchitra, M. R., Jaiganesh, K., and Parthasarathy, S. (2013) Diabetic Profile- Screening of HBA1C - A Random Community Assessment. *J Clin Diagn Res.*, *7*, 2200-2202. doi: 2210.7860/JCDR/2013/5690.3470. Epub 2013 Oct 2205. **D, A**

Susanto, H., Nesse, W., Dijkstra, P. U., Hoedemaker, E., van Reenen, Y. H., Agustina, D., Vissink, A., and Abbas, F. (2012) Periodontal inflamed surface area and C-reactive protein as predictors of HbA1c: a study in Indonesia. *Clin Oral Investig.*, *16*, 1237-1242. doi: 1210.1007/s00784-00011-00621-00780. Epub 02011 Oct 00720. **D, C**

Uruska, A., Araszkiewicz, A., Uruski, P., and Zozulinska-Ziolkiewicz, D. (2014) Higher risk of microvascular complications in smokers with type 1 diabetes despite intensive insulin therapy. Microvasc Res., 92:79-84., 10.1016/j.mvr.2014.1001.1002. Epub 2014 Jan 1012. **D, A**

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

Vlassopoulos, A., Lean, M. E., and Combet, E. (2013) Influence of smoking and diet on glycated haemoglobin and 'pre-diabetes' categorisation: a cross-sectional analysis. *BMC Public Health.*, *13:1013.*, 10.1186/1471-2458-1113-1013. **D, E**

Zhao, W., Katzmarzyk, P. T., Horswell, R., Wang, Y., Johnson, J., and Hu, G. (2014) HbA1c and heart failure risk among diabetic patients. *J Clin Endocrinol Metab.*, *99*, E263-267. doi: 210.1210/jc.2013-3325. Epub 2013 Jan 1211. **D, A**

Zhao, W., Katzmarzyk, P. T., Horswell, R., Wang, Y., Johnson, J., and Hu, G. (2014) HbA1c and coronary heart disease risk among diabetic patients. *Diabetes Care.*, *37*, 428-435. doi: 410.2337/dc2313-1525. Epub 2013 Oct 2315. **D, A**

Alexander, C. M., Landsman, P. B., Teutsch, S. M., and Haffner, S. M. (2003) NCEP-defined metabolic syndrome, diabetes, and prevalence of coronary heart disease among NHANES III participants age 50 years and older. *Diabetes.*, *52*, 1210-1214. **D**

Anan, F., Takahashi, N., Shinohara, T., Nakagawa, M., Masaki, T., Katsuragi, I., Tanaka, K., Kakuma, T., Yonemochi, H., Eshima, N., Saikawa, T., and Yoshimatsu, H. (2006) Smoking is associated with insulin resistance and cardiovascular autonomic dysfunction in type 2 diabetic patients. *Eur J Clin Invest.*, *36*, 459-465. **D**

Baggio, B., Budakovic, A., Dalla Vestra, M., Saller, A., Bruseghin, M., and Fioretto, P. (2002) Effects of cigarette smoking on glomerular structure and function in type 2 diabetic patients. *J Am Soc Nephrol.*, *13*, 2730-2736. **D**

Boeing, H., Weisgerber, U. M., Jeckel, A., Rose, H. J., and Kroke, A. (2000) Association between glycated hemoglobin and diet and other lifestyle factors in a nondiabetic population: cross-sectional evaluation of data from the Potsdam cohort of the European Prospective Investigation into Cancer and Nutrition Study. *Am J Clin Nutr.*, *71*, 1115-1122. **D, F**

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Cho, N. H., Chan, J. C., Jang, H. C., Lim, S., Kim, H. L., and Choi, S. H. (2009) Cigarette smoking is an independent risk factor for type 2 diabetes: a four-year community-based prospective study. *Clin Endocrinol (Oxf).* *71*, 679-685. doi: 610.1111/j.1365-2265.2009.03586.x. Epub 02009 Mar 03528. **D**

Clair, C., Bitton, A., Meigs, J. B., and Rigotti, N. A. (2011) Relationships of cotinine and self-reported cigarette smoking with hemoglobin A1c in the U.S.: results from the National Health and Nutrition Examination Survey, 1999-2008. *Diabetes Care.*, *34*, 2250-2255. doi: 2210.2337/dc2211-0710. Epub 2011 Aug 2211. **D, E, F**

Deepa, M., Pradeepa, R., Rema, M., Mohan, A., Deepa, R., Shanthirani, S., and Mohan, V. (2003) The Chennai Urban Rural Epidemiology Study (CURES)--study design and methodology (urban component) (CURES-I). *J Assoc Physicians India.*, *51*, 863-870. **D**

Dunstan, D. W., Zimmet, P. Z., Welborn, T. A., Cameron, A. J., Shaw, J., de Courten, M., Jolley, D., and McCarty, D. J. (2002) The Australian Diabetes, Obesity and Lifestyle Study (AusDiab)--methods and response rates. Diabetes Res Clin Pract., 57, 119-129. **D**

Fujimoto, W. Y., Leonetti, D. L., Kinyoun, J. L., Newell-Morris, L., Shuman, W. P., Stolov, W. C., and Wahl, P. W. (1987) Prevalence of diabetes mellitus and impaired glucose tolerance among second-generation Japanese-American men. Diabetes., 36, 721-729. **D**

Gerstein, H. C., Swedberg, K., Carlsson, J., McMurray, J. J., Michelson, E. L., Olofsson, B., Pfeffer, M. A., and Yusuf, S. (2008) The hemoglobin A1c level as a progressive risk factor for cardiovascular death, hospitalization for heart failure, or death in patients with chronic heart failure: an analysis of the Candesartan in Heart failure: Assessment of Reduction in Mortality and Morbidity (CHARM) program. Arch Intern Med., 168, 1699-1704. doi: 1610.1001/archinte.1168.1615.1699. **D, A**

Glumer, C., Jorgensen, T., and Borch-Johnsen, K. (2003) Prevalences of diabetes and impaired glucose regulation in a Danish population: the Inter99 study. *Diabetes Care.*, *26*, 2335-2340. **D**

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Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

Gulliford, M. C., and Ukoumunne, O. C. (2001) Determinants of glycated haemoglobin in the general population: associations with diet, alcohol and cigarette smoking. *Eur J Clin Nutr.*, *55*, 615-623. **D, E, F**

Herman, W. H., Ali, M. A., Aubert, R. E., Engelgau, M. M., Kenny, S. J., Gunter, E. W., Malarcher, A. M., Brechner, R. J., Wetterhall, S. F., DeStefano, F., and et al. (1995) Diabetes mellitus in Egypt: risk factors and prevalence. *Diabet Med.*, *12*, 1126-1131. **D**

Higgins, T., Cembrowski, G., Tran, D., Lim, E., and Chan, J. (2009) Influence of variables on hemoglobin A1c values and nonheterogeneity of hemoglobin A1c reference ranges. *J Diabetes Sci Technol.*, *3*, 644-648. **D**

Nilsson, P. M., Gudbjornsdottir, S., Eliasson, B., and Cederholm, J. (2004) Smoking is associated with increased HbA1c values and microalbuminuria in patients with diabetes--data from the National Diabetes Register in Sweden. *Diabetes Metab.*, *30*, 261-268. **D**

Nilsson, P. M., Lind, L., Pollare, T., Berne, C., and Lithell, H. O. (1995) Increased level of hemoglobin A1c, but not impaired insulin sensitivity, found in hypertensive and normotensive smokers. *Metabolism.*, *44*, 557-561. **D**

Pani, L. N., Korenda, L., Meigs, J. B., Driver, C., Chamany, S., Fox, C. S., Sullivan, L., D'Agostino, R. B., and Nathan, D. M. (2008) Effect of aging on A1C levels in individuals without diabetes: evidence from the Framingham Offspring Study and the National Health and Nutrition Examination Survey 2001-2004. *Diabetes Care.*, *31*, 1991-1996. doi: 1910.2337/dc1908-0577. Epub 2008 Jul 1915. **D**

Simon, D., Senan, C., Garnier, P., Saint-Paul, M., and Papoz, L. (1989) Epidemiological features of glycated haemoglobin A1c-distribution in a healthy population. The Telecom Study. *Diabetologia.*, *32*, 864-869. **D**

Smith, R. J., Koenig, R. J., Binnerts, A., Soeldner, J. S., and Aoki, T. T. (1982) Regulation of hemoglobin AIc formation in human erythrocytes in vitro. Effects of physiologic factors other than glucose. *J Clin Invest.*, *69*, 1164-1168. **D**

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Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

Soulimane, S., Simon, D., Shaw, J., Witte, D., Zimmet, P., Vol, S., Borch-Johnsen, K., Magliano, D., Vistisen, D., and Balkau, B. (2012) HbA1c, fasting plasma glucose and the prediction of diabetes: Inter99, AusDiab and D.E.S.I.R. *Diabetes Res Clin Pract.*, *96*, 392-399. doi: 310.1016/j.diabres.2011.1006.1003. Epub 2011 Jul 1017. **D**

Stengard, J. H., Tuomilehto, J., Pekkanen, J., Kivinen, P., Kaarsalo, E., Nissinen, A., and Karvonen, M. J. (1992) Diabetes mellitus, impaired glucose tolerance and mortality among elderly men: the Finnish cohorts of the Seven Countries Study. *Diabetologia.*, *35*, 760-765. **D**

Targher, G., Alberiche, M., Zenere, M. B., Bonadonna, R. C., Muggeo, M., and Bonora, E. (1997) Cigarette smoking and insulin resistance in patients with noninsulin-dependent diabetes mellitus. *J Clin Endocrinol Metab.*, *82*, 3619-3624. **D**

Voulgari, C., Katsilambros, N., and Tentolouris, N. (2011) Smoking cessation predicts amelioration of microalbuminuria in newly diagnosed type 2 diabetes mellitus: a 1-year prospective study. Metabolism., 60, 1456-1464. doi: 1410.1016/j.metabol.2011.1402.1014. Epub 2011 Apr 1412. **D, F**

Willi, C., Bodenmann, P., Ghali, W. A., Faris, P. D., and Cornuz, J. (2007) Active smoking and the risk of type 2 diabetes: a systematic review and meta-analysis. JAMA., 298, 2654-2664. **D**

Yudkin, J. S., Forrest, R. D., Jackson, C. A., Ryle, A. J., Davie, S., and Gould, B. J. (1990) Unexplained variability of glycated haemoglobin in non-diabetic subjects not related to glycaemia. Diabetologia., 33, 208-215. **D**

Zhou, X., Pang, Z., Gao, W., Wang, S., Zhang, L., Ning, F., Xue, B., Chen, X., and Qiao, Q. (2011) Fresh vegetable intake and prevalence of diabetes in a Chinese population in Qingdao. Diabetes Res Clin Pract., 92, 137-142. doi: 110.1016/j.diabres.2010.1012.1034. Epub 2011 Mar 1012. **D**

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7.6 Appendix 6 Inclusion criteria E

Ohkuma, T., Iwase, M., Fujii, H., Kaizu, S., Ide, H., Jodai, T., Kikuchi, Y., Idewaki, Y., Hirakawa, Y., Nakamura, U., and Kitazono, T. (2015) Dose- and time-dependent association of smoking and its cessation with glycemic control and insulin resistance in male patients with type 2 diabetes mellitus: the fukuoka diabetes registry. *PLoS One.*, *10*, e0122023. doi: 0122010.0121371/journal.pone.0122023. eCollection 0122015. **D, E, F**

Vlassopoulos, A., Lean, M. E., and Combet, E. (2013) Influence of smoking and diet on glycated haemoglobin and 'pre-diabetes' categorisation: a cross-sectional analysis. *BMC Public Health.*, *13:1013.*, 10.1186/1471-2458-1113-1013. **D, E**

Clair, C., Bitton, A., Meigs, J. B., and Rigotti, N. A. (2011) Relationships of cotinine and self-reported cigarette smoking with hemoglobin A1c in the U.S.: results from the National Health and Nutrition Examination Survey, 1999-2008. *Diabetes Care.*, *34*, 2250-2255. doi: 2210.2337/dc2211-0710. Epub 2011 Aug 2211. **D, E, F**

Gulliford, M. C., and Ukoumunne, O. C. (2001) Determinants of glycated haemoglobin in the general population: associations with diet, alcohol and cigarette smoking. *Eur J Clin Nutr.*, *55*, 615-623. **D, E, F**

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7.7 Appendix 7 Inclusion criteria F

Choi, Y. J., Park, J. S., Kim, U., Lee, S. H., Son, J. W., Shin, D. G., Kim, Y. J., Jeong, M. H., Ahn, Y. K., Cho, M. C., Bae, J. W., Kim, C. J., Cho, J. M., Han, K. R., and Lee, J. H. (2013) Changes in smoking behavior and adherence to preventive guidelines among smokers after a heart attack. *J Geriatr Cardiol.*, *10*, 146-150. doi: 110.3969/j.issn.1671-5411.2013.3902.3006. **F, A**

Ohkuma, T., Iwase, M., Fujii, H., Kaizu, S., Ide, H., Jodai, T., Kikuchi, Y., Idewaki, Y., Hirakawa, Y., Nakamura, U., and Kitazono, T. (2015) Dose- and time-dependent association of smoking and its cessation with glycemic control and insulin resistance in male patients with type 2 diabetes mellitus: the fukuoka diabetes registry. *PLoS One.*, *10*, e0122023. doi: 0122010.0121371/journal.pone.0122023. eCollection 0122015. **D, E, F**

Boeing, H., Weisgerber, U. M., Jeckel, A., Rose, H. J., and Kroke, A. (2000) Association between glycated hemoglobin and diet and other lifestyle factors in a nondiabetic population: cross-sectional evaluation of data from the Potsdam cohort of the European Prospective Investigation into Cancer and Nutrition Study. *Am J Clin Nutr.*, *71*, 1115-1122. **D, F**

Clair, C., Bitton, A., Meigs, J. B., and Rigotti, N. A. (2011) Relationships of cotinine and self-reported cigarette smoking with hemoglobin A1c in the U.S.: results from the National Health and Nutrition Examination Survey, 1999-2008. *Diabetes Care.*, *34*, 2250-2255. doi: 2210.2337/dc2211-0710. Epub 2011 Aug 2211. **D, E, F**

Gulliford, M. C., and Ukoumunne, O. C. (2001) Determinants of glycated haemoglobin in the general population: associations with diet, alcohol and cigarette smoking. *Eur J Clin Nutr.*, *55*, 615-623. **D, E, F**

Hokanson, J. M., Anderson, R. L., Hennrikus, D. J., Lando, H. A., and Kendall, D. M. (2006) Integrated tobacco cessation counseling in a diabetes self-management training program: a randomized trial of diabetes and reduction of tobacco. *Diabetes Educ.*, *32*, 562-570. **F**

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Voulgari, C., Katsilambros, N., and Tentolouris, N. (2011) Smoking cessation predicts amelioration of microalbuminuria in newly diagnosed type 2 diabetes mellitus: a 1-year prospective study. Metabolism., 60, 1456-1464. doi: 1410.1016/j.metabol.2011.1402.1014. Epub 2011 Apr 1412. **D, F**

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7.8 Appendix 8 Inclusion criteria G

No articles were identified with relevance to this inclusion criteria.

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7.9 Appendix 9 Review articles

Eliasson, B. (2003) Cigarette smoking and diabetes. *Prog Cardiovasc Dis.*, *45*, 405-413. **R**

Ahmad, J., and Rafat, D. (2013) HbA1c and iron deficiency: a review. *Diabetes Metab Syndr.*, *7*, 118-122. doi: 110.1016/j.dsx.2013.1002.1004. Epub 2013 Mar 1015. **R**

Barth, J. H., Marshall, S. M., and Watson, I. D. (2008) Consensus meeting on reporting glycated haemoglobin (HbA1c) and estimated average glucose (eAG) in the UK: report to the National Director for Diabetes, Department of Health. *Diabet Med.*, *25*, 381-382. doi: 310.1111/j.1464-5491.2008.02436.x. **R**

Benhalima, K., Standl, E., and Mathieu, C. (2011) The importance of glycemic control: how low should we go with HbA1c? Start early, go safe, go low. *J Diabetes Complications.*, *25*, 202-207. doi: 210.1016/j.jdiacomp.2010.1003.1002. Epub 2010 May 1011. **R**

Carter, P., Achana, F., Troughton, J., Gray, L. J., Khunti, K., and Davies, M. J. (2014) A Mediterranean diet improves HbA1c but not fasting blood glucose compared to alternative dietary strategies: a network meta-analysis. *J Hum Nutr Diet.*, *27*, 280-297. doi: 210.1111/jhn.12138. Epub 12013 Jun 12122. **R**

Chetty, V. T., Almulla, A., Odueyungbo, A., and Thabane, L. (2008) The effect of continuous subcutaneous glucose monitoring (CGMS) versus intermittent whole blood finger-stick glucose monitoring (SBGM) on hemoglobin A1c (HBA1c) levels in Type I diabetic patients: a systematic review. Diabetes Res Clin Pract., 81, 79-87. doi: 10.1016/j.diabres.2008.1002.1014. Epub 2008 Apr 1015**. R**

Cohen, R. M., and Smith, E. P. (2008) Frequency of HbA1c discordance in estimating blood glucose control. Curr Opin Clin Nutr Metab Care., 11, 512-517. doi: 510.1097/MCO.1090b1013e32830467bd. **R**

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DeFronzo, R. A., Stonehouse, A. H., Han, J., and Wintle, M. E. (2010) Relationship of baseline HbA1c and efficacy of current glucose-lowering therapies: a meta-analysis of randomized clinical trials. *Diabet Med.*, *27*, 309-317. doi: 310.1111/j.1464-5491.2010.02941.x. **R**

Florkowski, C. (2013) HbA1c as a Diagnostic Test for Diabetes Mellitus - Reviewing the Evidence. *Clin Biochem Rev.*, *34*, 75-83. **R**

Gillery, P. (2000) [Strengths and limitations of Hba1c determination. The point of view of the biologist]. *Journ Annu Diabetol Hotel Dieu*, 195-201. **R**

Heinemann, L., and Freckmann, G. (2015) Quality of HbA1c Measurement in the Practice: The German Perspective. *J Diabetes Sci Technol*, *17*, 1932296815572254. **R**

Higgins, T. (2013) HbA1c for screening and diagnosis of diabetes mellitus. *Endocrine.*, *43*, 266-273. doi: 210.1007/s12020-12012-19768-y. Epub 12012 Aug 12021. **R**

Hoelzel, W., and Miedema, K. (1996) Development of a reference system for the international standardization of HbA1c/glycohemoglobin determinations. *J Int Fed Clin Chem*, *1996 Jun;8*, 62-64. **R**

Jazet, I. M., and Meinders, A. E. (2009) Glucoregulation in type 2 diabetes: the lower the better? Glycosylated HbA1c of 6.5% seems to be the limit. *Eur J Intern Med.*, *20*, 232-235. doi: 210.1016/j.ejim.2008.1008.1002. Epub 2008 Sep 1014. **R**

Juarez, D. T., Demaris, K. M., Goo, R., Mnatzaganian, C. L., and Wong Smith, H. (2014) Significance of HbA1c and its measurement in the diagnosis of diabetes mellitus: US experience. *Diabetes Metab Syndr Obes.*, *7:487-94.*, 10.2147/DMSO.S39092. eCollection 32014. **R**

Kirk, J. K., D'Agostino, R. B., Jr., Bell, R. A., Passmore, L. V., Bonds, D. E., Karter, A. J., and Narayan, K. M. (2006) Disparities in HbA1c levels between African-American and non-Hispanic white adults with diabetes: a meta-analysis. Diabetes Care., 29, 2130-2136. **R**

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Kowall, B., and Rathmann, W. (2013) HbA1c for diagnosis of type 2 diabetes. Is there an optimal cut point to assess high risk of diabetes complications, and how well does the 6.5% cutoff perform? *Diabetes Metab Syndr Obes.*, *6:477-91.*, 10.2147/DMSO.S39093. **R, A**

Kurukulasuriya, L. R., and Sowers, J. R. (2010) Therapies for type 2 diabetes: lowering HbA1c and associated cardiovascular risk factors. *Cardiovasc Diabetol.*, *9:45.*, 10.1186/1475-2840-1189-1145. **R, A**

Lai, L. C. (2008) Global standardisation of HbA1c. *Malays J Pathol.*, *30*, 67-71. **R**

Landgraf, R. (2004) The relationship of postprandial glucose to HbA1c. *Diabetes Metab Res Rev.*, *20*, S9-S12. **R**

Lefebvre, P. (2000) [Strengths and limitations of Hba1c determination: the point of view of the clinician]. *Journ Annu Diabetol Hotel Dieu*, 203-210. **R**

Letourneau, J., Bui, H., Schricker, T., and Hatzakorzian, R. (2013) HbA1c: a prognostic biomarker in the surgical and critically ill patient population. *J Cardiothorac Vasc Anesth.*, *27*, 760-764. doi: 710.1053/j.jvca.2012.1006.1030. Epub 2012 Aug 1031. **R, A**

Liew, A. K., Punnanithinont, N., Lee, Y. C., and Yang, J. (2013) Effect of non-surgical periodontal treatment on HbA1c: a meta-analysis of randomized controlled trials. *Aust Dent J.*, *58*, 350-357. doi: 310.1111/adj.12091. **R, C**

Little, R. R., and Rohlfing, C. L. (2013) The long and winding road to optimal HbA1c measurement. *Clin Chim Acta.*, *418:63-71.*, 10.1016/j.cca.2012.1012.1026. Epub 2013 Jan 1011. **R**

Little, R. R., and Sacks, D. B. (2009) HbA1c: how do we measure it and what does it mean? *Curr Opin Endocrinol Diabetes Obes.*, *16*, 113-118. doi: 110.1097/MED.1090b1013e328327728d. **R**

Manley, S. E. (2008) Estimated average glucose derived from HbA1c eAG: report from European Association for the Study of Diabetes (EASD), Amsterdam 2007. *Diabet Med.*, *25*, 126-128. doi: 110.1111/j.1464-5491.2008.02383.x. **R**

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Marre, M. (1998) [Which HbA1c to look at?]. Journ Annu Diabetol Hotel Dieu, 249-256. **R**

Marshall, S. M., and Barth, J. H. (2000) Standardization of HbA1c measurements--a consensus statement. *Diabet Med.*, *17*, 5-6. **R**

Mostafa, S. A., Davies, M. J., Srinivasan, B. T., Carey, M. E., Webb, D., and Khunti, K. (2010) Should glycated haemoglobin (HbA1c) be used to detect people with type 2 diabetes mellitus and impaired glucose regulation? *Postgrad Med J.*, *86*, 656-662. doi: 610.1136/pgmj.2009.091215. Epub 092010 Oct 091218. **R**

Nitin, S. (2010) HbA1c and factors other than diabetes mellitus affecting it. *Singapore Med J.*, *51*, 616-622. **R**

Procopiou, M. (2006) [HbA1c: review and recent developments]. Rev Med Suisse, 2006 May 31;2, 1473-1474. **R**

Punales, M. K., Geremia, C., Mondadori, P., Pickler, M., Fornari, A., and Tschiedel, B. (2008) [How the continuous glucose monitoring system can contribute to HbA1c interpretation in type 1 diabetes mellitus?]. Arq Bras Endocrinol Metabol., 52, 299-306. **R**

Reynolds, T. M., Smellie, W. S., and Twomey, P. J. (2006) Glycated haemoglobin (HbA1c) monitoring. *BMJ.*, *333*, 586-588. **R**

Rollins, K. E., Varadhan, K. K., Dhatariya, K., and Lobo, D. N. (2015) Systematic review of the impact of HbA1c on outcomes following surgery in patients with diabetes mellitus. *Clin Nutr*, *17*, 00082-00085. **R, C**

Roszyk, L., Faye, B., Sapin, V., Somda, F., and Tauveron, I. (2007) Glycated haemoglobin (HbA1c): today and tomorrow. *Ann Endocrinol (Paris). 68*, 357-365. Epub 2007 Sep 2029. **R**

Schnedl, W. J., Liebminger, A., Roller, R. E., Lipp, R. W., and Krejs, G. J. (2001) Hemoglobin variants and determination of glycated hemoglobin (HbA1c). *Diabetes Metab Res Rev.*, *17*, 94-98. **R**

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Seitz, P., Rosemann, T., Gensichen, J., and Huber, C. A. (2011) Interventions in primary care to improve cardiovascular risk factors and glycated haemoglobin (HbA1c) levels in patients with diabetes: a systematic review. *Diabetes Obes Metab.*, *13*, 479-489. doi: 410.1111/j.1463-1326.2010.01347.x. **R, A**

Stettler, C., Mueller, B., and Diem, P. (2000) [What you always wanted to know about HbA1c]. *Schweiz Med Wochenschr.*, *130*, 993-1005. **R**

Sturm, G., Lamina, C., Zitt, E., Lhotta, K., Haider, F., Neyer, U., and Kronenberg, F. (2011) Association of HbA1c values with mortality and cardiovascular events in diabetic dialysis patients. The INVOR study and review of the literature. *PLoS One*, *6*, e20093. doi: 20010.21371/journal.pone.0020093. Epub 0022011 May 0020018. **R, A, C**

ten Brinke, R., Dekker, N., de Groot, M., and Ikkersheim, D. (2008) Lowering HbA1c in type 2 diabetics results in reduced risk of coronary heart disease and all-cause mortality. *Prim Care Diabetes.*, *2*, 45-49. doi: 10.1016/j.pcd.2007.1012.1004. Epub 2008 Feb 1018. **R, A, C**

Tennyson, C., Lee, R., and Attia, R. (2013) Is there a role for HbA1c in predicting mortality and morbidity outcomes after coronary artery bypass graft surgery? *Interact Cardiovasc Thorac Surg.*, *17*, 1000-1008. doi: 1010.1093/icvts/ivt1351. Epub 2013 Sep 1010. **R, A**

Umpierre, D., Ribeiro, P. A., Kramer, C. K., Leitao, C. B., Zucatti, A. T., Azevedo, M. J., Gross, J. L., Ribeiro, J. P., and Schaan, B. D. (2011) Physical activity advice only or structured exercise training and association with HbA1c levels in type 2 diabetes: a systematic review and meta-analysis. JAMA., 305, 1790-1799. doi: 1710.1001/jama.2011.1576. **R, A, C**

Valentine, W. J., Palmer, A. J., Nicklasson, L., Cobden, D., and Roze, S. (2006) Improving life expectancy and decreasing the incidence of complications associated with type 2 diabetes: a modelling study of HbA1c targets. Int J Clin Pract., 60, 1138-1145. **R**

Weykamp, C. (2013) HbA1c: a review of analytical and clinical aspects. *Ann Lab Med.*, *33*, 393-400. doi: 310.3343/alm.2013.3333.3346.3393. Epub 2013 Oct 3317. **R**

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Lecube, A., Sampol, G., Munoz, X., Hernandez, C., Mesa, J., and Simo, R. (2010) Type 2 diabetes impairs pulmonary function in morbidly obese women: a case-control study. *Diabetologia.*, *53*, 1210-1216. doi: 1210.1007/s00125-00010-01700-00125. Epub 02010 Mar 00129. **R**

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7.10 Appendix 10 Excluded articles

01 No usable data or information on HbA1c were presented

Bordas-Fonfrede, M., Selam, J., Goudable, J., Thivolet, C., Vialettes, B., Chapelle, J., Drouin, P., Hue, G., Levy-

Marchal, C., Slama, G., and Gillery, P. (2000) [Considerations on delocalized HbA1c assays]. *Diabetes Metab.*, *26*, 508-512. **01**

Bryskiewicz, M. E., and Majkowska, L. (2011) [Aspects of the standardization of glycated hemoglobin (HbA1c) measurement]. *Pol Merkur Lekarski.*, *30*, 155-159. **01**

Cerami, C., Founds, H., Nicholl, I., Mitsuhashi, T., Giordano, D., Vanpatten, S., Lee, A., Al-Abed, Y., Vlassara, H., Bucala, R., and Cerami, A. (1997) Tobacco smoke is a source of toxic reactive glycation products. *Proc Natl Acad Sci U S A.*, *94*, 13915-13920. **01**

Christensen, D. L., Friis, H., Mwaniki, D. L., Kilonzo, B., Tetens, I., Boit, M. K., Omondi, B., Kaduka, L., and Borch-Johnsen, K. (2009) Prevalence of glucose intolerance and associated risk factors in rural and urban populations of different ethnic groups in Kenya. *Diabetes Res Clin Pract.*, *84*, 303-310. doi: 310.1016/j.diabres.2009.1003.1007. Epub 2009 Apr 1019. **01**

Dorchy, H. (2015) One center in Brussels has consistently had the lowest HbA1c values in the 4 studies (1994-2009) by the Hvidoere International Study Group on Childhood Diabetes: What are the "recipes"? *World J Diabetes.*, *6*, 1-7. doi: 10.4239/wjd.v4236.i4231.4231. **01**

Halmai, R., Degrell, P., Szijarto, I. A., Matyas, V., Molnar, G. A., Kovacs, T., and Wittmann, I. (2013) Smoking as the potential link between Kimmelstiel-Wilson lesion and non-diabetic nodular glomerulosclerosis in male patients - a single center retrospective study. *Clin Nephrol.*, *80*, 23-28. doi: 10.5414/CN107812. **01**

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

Harvey, P. W., Petkov, J., Kowanko, I., Helps, Y., and Battersby, M. (2013) Chronic condition management and self-management in Aboriginal communities in South Australia: outcomes of a longitudinal study. *Aust Health Rev.*, *37*, 246-250. doi: 210.1071/AH12165. **01**

Kashiwagi, A. (2013) [Development of the HbA1c international standardization of HbA1c measurement in Japan Diabetes Society]. *Rinsho Byori.*, *61*, 585-593. **01**

Kawahara, R. (1998) [Glycohemoglobin (HbA1c, HbA1)]. *Nihon Rinsho.*, *56*, 55-58. **01**

Kawahara, R. (1999) [Glycohemoglobin (HbA1c, HbA1)]. *Nihon Rinsho.*, *57*, 615-617. **01**

Lipska, K. J., Inzucchi, S. E., Van Ness, P. H., Gill, T. M., Kanaya, A., Strotmeyer, E. S., Koster, A., Johnson, K. C., Goodpaster, B. H., Harris, T., and De Rekeneire, N. (2013) Elevated HbA1c and fasting plasma glucose in predicting diabetes incidence among older adults: are two better than one? *Diabetes Care.*, *36*, 3923-3929. doi: 3910.2337/dc3912-2631. Epub 2013 Oct 3917. **01**

Madar, A. A., Knutsen, K. V., Stene, L. C., Brekke, M., Meyer, H. E., and Lagerlov, P. (2014) Effect of vitamin D3 supplementation on glycated hemoglobin (HbA1c), fructosamine, serum lipids, and body mass index: a randomized, double-blinded, placebo-controlled trial among healthy immigrants living in Norway. *BMJ Open Diabetes Res Care.*, *2*, e000026. doi: 000010.001136/bmjdrc-002014-000026. eCollection 002014. **01**

Shima, K., and Kuwajima, M. (1998) [Standardization for glycohemoglobin (HbA1c) measurements and its evaluation]. *Nihon Rinsho.*, *56*, 59-67. **01**

Tominaga, M. (2002) [Hemoglobin A1c (HbA1c)]. *Nihon Rinsho.*, *60*, 405-409. **01**

02 Clinical study with patients, focus on diagnosis, therapy and prognosis

Aoki, Y. (2013) [Approach to the changes of HbA1c notation in health checkups]. *Rinsho Byori.*, *61*, 607-611. **02**

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

Bryskiewicz, M. E., and Majkowska, L. (2011) [Glycated hemoglobin (HbA1c) as a standard diagnostic criterium for diabetes?]. *Pol Merkur Lekarski.*, *30*, 150-154. **02**

Casparie, A. F., and Miedema, K. (1980) [HBA1c and diabetes mellitus]. *Ned Tijdschr Geneeskd.*, *124*, 930-934. **02**

Doggrell, S. A., and Warot, S. (2014) The association between the measurement of adherence to anti-diabetes medicine and the HbA1c. *Int J Clin Pharm.*, *36*, 488-497. doi: 410.1007/s11096-11014-19929-11096. Epub 12014 Mar 11022. **02**

Esposito, K., Chiodini, P., Bellastella, G., Maiorino, M. I., and Giugliano, D. (2012) Proportion of patients at HbA1c target <7% with eight classes of antidiabetic drugs in type 2 diabetes: systematic review of 218 randomized controlled trials with 78 945 patients. *Diabetes Obes Metab.*, *14*, 228-233. doi: 210.1111/j.1463-1326.2011.01512.x. Epub 02011 Nov 01513. **02**

Giugliano, D., Maiorino, M., Bellastella, G., Chiodini, P., and Esposito, K. (2011) Relationship of baseline HbA1c, HbA1c change and HbA1c target of < 7% with insulin analogues in type 2 diabetes: a meta-analysis of randomised controlled trials. *Int J Clin Pract.*, *65*, 602-612. doi: 610.1111/j.1742-1241.2010.02619.x. **02**

Giugliano, D., Maiorino, M. I., Bellastella, G., Chiodini, P., and Esposito, K. (2011) Multiple HbA1c targets and insulin analogues in type 2 diabetes: a systematic review. *J Diabetes Complications.*, *25*, 275-281. doi: 210.1016/j.jdiacomp.2011.1003.1005. Epub 2011 May 1020. **02**

Hirst, J. A., Farmer, A. J., Dyar, A., Lung, T. W., and Stevens, R. J. (2013) Estimating the effect of sulfonylurea on HbA1c in diabetes: a systematic review and meta-analysis. *Diabetologia.*, *56*, 973-984. doi: 910.1007/s00125-00013-02856-00126. Epub 02013 Mar 00115. **02**

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

Jones, A., Gladstone, B. P., Lubeck, M., Lindekilde, N., Upton, D., and Vach, W. (2014) Motivational interventions in the management of HbA1c levels: a systematic review and meta-analysis. *Prim Care Diabetes.*, *8*, 91-100. doi: 110.1016/j.pcd.2014.1001.1009. Epub 2014 Feb 1010. **02**

LaSalle, J. R. (2010) Reaching HbA1c goals with saxagliptin in combination with other oral antidiabetic drugs. *Postgrad Med.*, *122*, 144-152. doi: 110.3810/pgm.2010.3801.2108. **02**

Lieber, B. A., Taylor, B., Appelboom, G., Prasad, K., Bruce, S., Yang, A., Bruce, E., Christophe, B., and Connolly, E. S., Jr. (2015) Meta-analysis of telemonitoring to improve HbA1c levels: Promise for stroke survivors. *J Clin Neurosci*, *16*, 00706-00701. **02**

Mavian, A. A., Miller, S., and Henry, R. R. (2010) Managing type 2 diabetes: balancing HbA1c and body weight. *Postgrad Med.*, *122*, 106-117. doi: 110.3810/pgm.2010.3805.2148. **02**

Moona, M. M., Smits, R., Kertesz, J., Meyer, A., and Mackler, L. (2014) Clinical inquiry: do complementary agents lower HbA1c when used with standard type 2 diabetes therapy? *J Fam Pract.*, *63*, 336-338. **02**

Ngiam, K. Y., Lee, W. J., Lee, Y. C., and Cheng, A. (2014) Efficacy of metabolic surgery on HbA1c decrease in type 2 diabetes mellitus patients with BMI <35 kg/m2--a review. *Obes Surg.*, *24*, 148-158. doi: 110.1007/s11695-11013-11112-y. **02**

Nishio, Y. (2013) [New era of laboratory testing. Topics: II. Particulars; 1. Clinical laboratory test for diabetes: topics in HbA1c]. *Nihon Naika Gakkai Zasshi.*, *102*, 3110-3116. **02**

Osawa, H., Onuma, H., and Makino, H. (2005) [Combined use of fasting plasma glucose and HbA1c (as a screening test)]. *Nihon Rinsho.*, *63*, 390-393. **02**

Sato, A. (2014) [Indicators of glycemic control --hemoglobin A1c (HbA1c), glycated albumin (GA), and 1,5-anhydroglucitol (1,5-AG)]. *Rinsho Byori.*, *62*, 45-52. **02**

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

Tahara, Y., and Shima, K. (2005) [Analysis of HbA1c and glycoalbumin for diagnosis of impaired glucose tolerance]. *Nihon Rinsho.*, *63*, 382-385. **02**

Tominaga, M. (2003) [Diabetes mellitus and HbA1c]. *Rinsho Byori.*, *51*, 586-591. **02**

Toth, L., Szenasi, P., Kammerer, L., and Romics, L. (1990) [Correlation of thrombocyte reactivity and serum levels of HbA1c, cholesterol and creatinine in diabetes mellitus]. *Orv Hetil*, *1990 Feb 25;131*, 405-406. **02**

Yagame, M., Jinde, K., Suzuki, D., Saotome, N., Takano, H., Tanabe, R., Sato, H., Kurokawa, K., Sakai, H., Matsumae, M., Mase, H., and Harano, T. (1997) A diabetic case with hemoglobin J-Meerut and low HbA1C levels. *Intern Med.*, *36*, 351-356. **02**

Yan, S., Liu, S., Zhao, Y., Zhang, W., Sun, X., Li, J., Jiang, F., Ju, J., Lang, N., Zhang, Y., Zhou, W., and Li, Q. (2013) Diagnostic accuracy of HbA1c in diabetes between Eastern and Western. *Eur J Clin Invest.*, *43*, 716-726. doi: 710.1111/eci.12098. Epub 12013 May 12092. **02**

Arai, K., Hirao, K., Yamauchi, M., Kobayashi, M., and Kashiwagi, A. (2013) Short duration of diabetes and disuse of sulfonylurea have any association with insulin cessation of the patients with type 2 diabetes in a clinical setting in Japan (JDDM 30). *Endocr J*, *60*, 305-310. Epub 2012 Nov 2010. **02**

Fan, H. Q., Tang, W., Wang, Z. X., Wang, S. J., Qin, Y. H., Fu, Q., Gao, Y., Sun, M., Zhang, M., Zhou, H. W., and Yang, T. (2013) Association of serum uric acid with 2-hour postload glucose in Chinese with impaired fasting plasma glucose and/or HbA1c. PLoS One., 8, e67759. doi: 67710.61371/journal.pone.0067759. Print 0062013. **02**

Govan, L., Maietti, E., Torsney, B., Wu, O., Briggs, A., Colhoun, H. M., Fischbacher, C. M., Leese, G. P., McKnight, J. A., Morris, A. D., Sattar, N., Wild, S. H., and Lindsay, R. S. (2012) The effect of deprivation and HbA1c on admission to hospital for diabetic ketoacidosis in type 1 diabetes. Diabetologia., 55, 2356-2360. Epub 2012 Jun 2326. **02**

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

Hou, X., Wang, C., Wang, S., Yang, W., Ma, Z., Wang, Y., Li, C., Li, M., Zhang, X., Zhao, X., Sun, Y., Song, J., Lin, P., Liang, K., Gong, L., Wang, M., Liu, F., Li, W., Yan, F., Yang, J., Wang, L., Tian, M., Liu, J., Zhao, R., Chen, S., and Chen, L. (2014) Fluctuation between fasting and 2-H postload glucose state is associated with glomerular hyperfiltration in newly diagnosed diabetes patients with HbA1c < 7%. *PLoS One.*, *9*, e111173. doi: 111110.111371/journal.pone.0111173. eCollection 0112014. **02**

Madden, T. E., Herriges, B., Boyd, L. D., Laughlin, G., Chiodo, G., and Rosenstein, D. (2008) Alterations in HbA1c following minimal or enhanced non-surgical, non-antibiotic treatment of gingivitis or mild periodontitis in type 2 diabetic patients: a pilot trial. *J Contemp Dent Pract.*, *9*, 9-16. **02**

Orban, T., Bundy, B., Becker, D. J., Dimeglio, L. A., Gitelman, S. E., Goland, R., Gottlieb, P. A., Greenbaum, C. J., Marks, J. B., Monzavi, R., Moran, A., Peakman, M., Raskin, P., Russell, W. E., Schatz, D., Wherrett, D. K., Wilson, D. M., Krischer, J. P., and Skyler, J. S. (2014) Costimulation modulation with abatacept in patients with recent-onset type 1 diabetes: follow-up 1 year after cessation of treatment. *Diabetes Care.*, *37*, 1069-1075. doi: 1010.2337/dc1013-0604. Epub 2013 Dec 1062. **02**

Shah, A. D., Fox, R. K., and Rushakoff, R. J. (2014) Falsely Decreased HbA1c in a Type 2 Diabetic Patient Treated with Dapsone. *Endocr Pract.*, *20*, e229-232. doi: 210.4158/EP14291.CR. **02**

Suljic, E., Kulasin, I., and Alibegovic, V. (2013) Assessment of Diabetic Polyneuropathy in Inpatient Care: Fasting Blood Glucose, HbA1c, Electroneuromyography and Diabetes Risk Factors. *Acta Inform Med*, *21*, 123-126. doi: 110.5455/aim.2013.5421.5123-5126. **02**

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

Sun, Y., Wang, C., Yang, W., Wang, Y., Zhang, X., Ma, Z., Song, J., Lin, P., Liang, K., Ma, A., Zheng, H., Wu, J., Gong, L., Wang, M., Liu, F., Li, W., Yan, F., Yang, J., Wang, L., Tian, M., Liu, J., Zhao, R., Hou, X., and Chen, L. (2015) Fasting blood glucose, but not 2-h postload blood glucose or HbA1c, is associated with mild decline in estimated glomerular filtration rate in healthy Chinese. *Int Urol Nephrol.*, *47*, 147-152. doi: 110.1007/s11255-11014-10880-11251. Epub 12014 Dec 11211. **02**

(2013) HbA1c targets in type 2 diabetes: guidelines and evidence. *Drug Ther Bull.*, *51*, 42-45. doi: 10.1136/dtb.2013.1134.0172. Epub 2013 Apr 1133. **02**

Bernal-Lopez, M. R., Villalobos-Sanchez, A., Mancera-Romero, J., Jansen-Chaparro, S., Baca-Osorio, A. J., Lopez-Carmona, M. D., Tinahones, F. J., and Gomez-Huelgas, R. (2011) Why not use the HbA1c as a criterion of dysglycemia in the new definition of the metabolic syndrome? Impact of the new criteria in the prevalence of the metabolic syndrome in a Mediterranean urban population from Southern Europe (IMAP study. Multidisciplinary intervention in primary care). *Diabetes Res Clin Pract.*, *93*, e57-60. doi: 10.1016/j.diabres.2011.1002.1024. Epub 2011 Mar 1021. **02**

Kesim, M., Tiryaki, A., Kadioglu, M., Muci, E., Kalyoncu, N. I., and Yaris, E. (2011) The effects of sertraline on blood lipids, glucose, insulin and HBA1C levels: A prospective clinical trial on depressive patients. *J Res Med Sci.*, *16*, 1525-1531. **02**

Lind, M., Tuomilehto, J., Uusitupa, M., Nerman, O., Eriksson, J., Ilanne-Parikka, P., Keinanen-Kiukaanniemi, S., Peltonen, M., Pivodic, A., and Lindstrom, J. (2014) The association between HbA1c, fasting glucose, 1-hour glucose and 2-hour glucose during an oral glucose tolerance test and cardiovascular disease in individuals with elevated risk for diabetes. *PLoS One.*, *9*, e109506. doi: 109510.101371/journal.pone.0109506. eCollection 0102014. **02**

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

Varvel, S. A., Voros, S., Thiselton, D. L., Pottala, J. V., Dall, T., Warnick, G. R., McConnell, J. P., Ghaedi, L., Sasinowski, M., and Graham, T. (2014) Comprehensive biomarker testing of glycemia, insulin resistance, and beta cell function has greater sensitivity to detect diabetes risk than fasting glucose and HbA1c and is associated with improved glycemic control in clinical practice. J Cardiovasc Transl Res., 7, 597-606. doi: 510.1007/s12265-12014-19577-12261. Epub 12014 Jul 12229. **02**

Wami, W. M., Buntinx, F., Bartholomeeusen, S., Goderis, G., Mathieu, C., and Aerts, M. (2013) Influence of chronic comorbidity and medication on the efficacy of treatment in patients with diabetes in general practice. *Br J Gen Pract.*, *63*, e267-273. doi: 210.3399/bjgp3313X665233. **02**

Fowke, J. H., Matthews, C. M., Buchowski, M. S., Signorello, L. B., Chang, S. S., Cookson, M. S., and Blot, W. J. (2008) Association between prostate-specific antigen and leptin, adiponectin, HbA1c or C-peptide among African-American and Caucasian men. Prostate Cancer Prostatic Dis, 11, 264-269. Epub 2007 Oct 2016. **02**

Ozbek, E., Otunctemur, A., Dursun, M., Sahin, S., Besiroglu, H., Koklu, I., Erkoc, M., Danis, E., and Bozkurt, M. (2014) Diabetes mellitus and HbA1c levels associated with high grade prostate cancer. *Asian Pac J Cancer Prev*, *15*, 2555-2558. **02**

Balkau, B., Lange, C., Fezeu, L., Tichet, J., de Lauzon-Guillain, B., Czernichow, S., Fumeron, F., Froguel, P., Vaxillaire, M., Cauchi, S., Ducimetiere, P., and Eschwege, E. (2008) Predicting diabetes: clinical, biological, and genetic approaches: data from the Epidemiological Study on the Insulin Resistance Syndrome (DESIR). *Diabetes Care.*, *31*, 2056-2061. doi: 2010.2337/dc2008-0368. Epub 2008 Aug 2058. **02**

03 Population investigated is not relevant for the purpose of this document (e.g. children, pregnant women, ill persons)

Bottermann, P. (2009) [HbA1c 8.5% in elderly people with diabetes: is it good enough?]. *MMW Fortschr Med.*, *151*, 38-39. **03**

Chamnan, P., Simmons, R. K., Forouhi, N. G., Luben, R. N., Khaw, K. T., Wareham, N. J., and Griffin, S. J. (2011) Incidence of type 2 diabetes using proposed HbA1c

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

diagnostic criteria in the european prospective investigation of cancer-norfolk cohort: implications for preventive strategies. Diabetes Care., 34, 950-956. doi: 910.2337/dc2309-2326. Epub 2010 Jul 2339. **03**

Cohen, H. W., Crandall, J. P., Hailpern, S. M., and Billett, H. H. (2008) Aspirin resistance associated with HbA1c and obesity in diabetic patients. *J Diabetes Complications.*, *22*, 224-228. doi: 210.1016/j.jdiacomp.2007.1005.1002. Epub 2008 Apr 1016. **03**

Colagiuri, S., Colagiuri, R., Na'ati, S., Muimuiheata, S., Hussain, Z., and Palu, T. (2002) The prevalence of diabetes in the kingdom of Tonga. *Diabetes Care.*, *25*, 1378-1383. **03**

Hara, M., Higaki, Y., Taguchi, N., Shinchi, K., Morita, E., Naito, M., Hamajima, N., Takashima, N., Suzuki, S., Nakamura, A., Ohnaka, K., Uemura, H., Nishida, H., Hosono, S., Mikami, H., Kubo, M., and Tanaka, H. (2012) Effect of the PPARG2 Pro12Ala polymorphism and clinical risk factors for diabetes mellitus on HbA1c in the Japanese general population. *J Epidemiol*, *22*, 523-531. doi: 510.2188/jea.JE20120078. Epub 20122012 Sep 20120022. **03**

Javed, F., Al-Kheraif, A. A., Al Amri, M. D., Alshehri, M., Vohra, F., Al-Askar, M., Malmstrom, H., and Romanos, G. E. (2015) Periodontal Status and Whole Salivary Cytokine Profile Among Smokers and Never-Smokers With and Without Prediabetes. *J Periodontol*, *12*, 1-15. **03**

Lapolla, A., Dalfra, M. G., and Fedele, D. (2010) Pregnancy complicated by diabetes: what is the best level of HbA1c for conception? *Acta Diabetol.*, *47*, 187-192. doi: 110.1007/s00592-00010-00199-z. Epub 02010 May 00526. **03**

Murphy, C. V., Coffey, R., Wisler, J., and Miller, S. F. (2013) The relationship between acute and chronic hyperglycemia and outcomes in burn injury. *J Burn Care Res.*, *34*, 109-114. doi: 110.1097/BCR.1090b1013e3182700025. **03**

Nakhjavani, M., Esteghamati, A., Esfahanian, F., Ghanei, A., Rashidi, A., and Hashemi, S. (2008) HbA1c negatively correlates with LCAT activity in type 2 diabetes. Diabetes

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International.

Res Clin Pract., 81, 38-41. doi: 10.1016/j.diabres.2008.1001.1018. Epub 2008 May 1015. **03**

Oghagbon, E. K. (2014) Commentary: improving persistently elevated HbA1c in diabetes mellitus patients in Nigeria. *Ethn Dis.*, *24*, 502-507. **03**

Rafat, D., and Ahmad, J. (2012) HbA1c in pregnancy. Diabetes Metab Syndr., 6, 59-64. doi: 10.1016/j.dsx.2012.1005.1010. Epub 2012 Jun 1030. **03**

Siddiqui, A. A., Maddur, H., Naik, S., and Cryer, B. (2008) The association of elevated HbA1c on the behavior of adenomatous polyps in patients with type-II diabetes mellitus. *Dig Dis Sci.*, *53*, 1042-1047. Epub 2007 Oct 1016. **03**

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