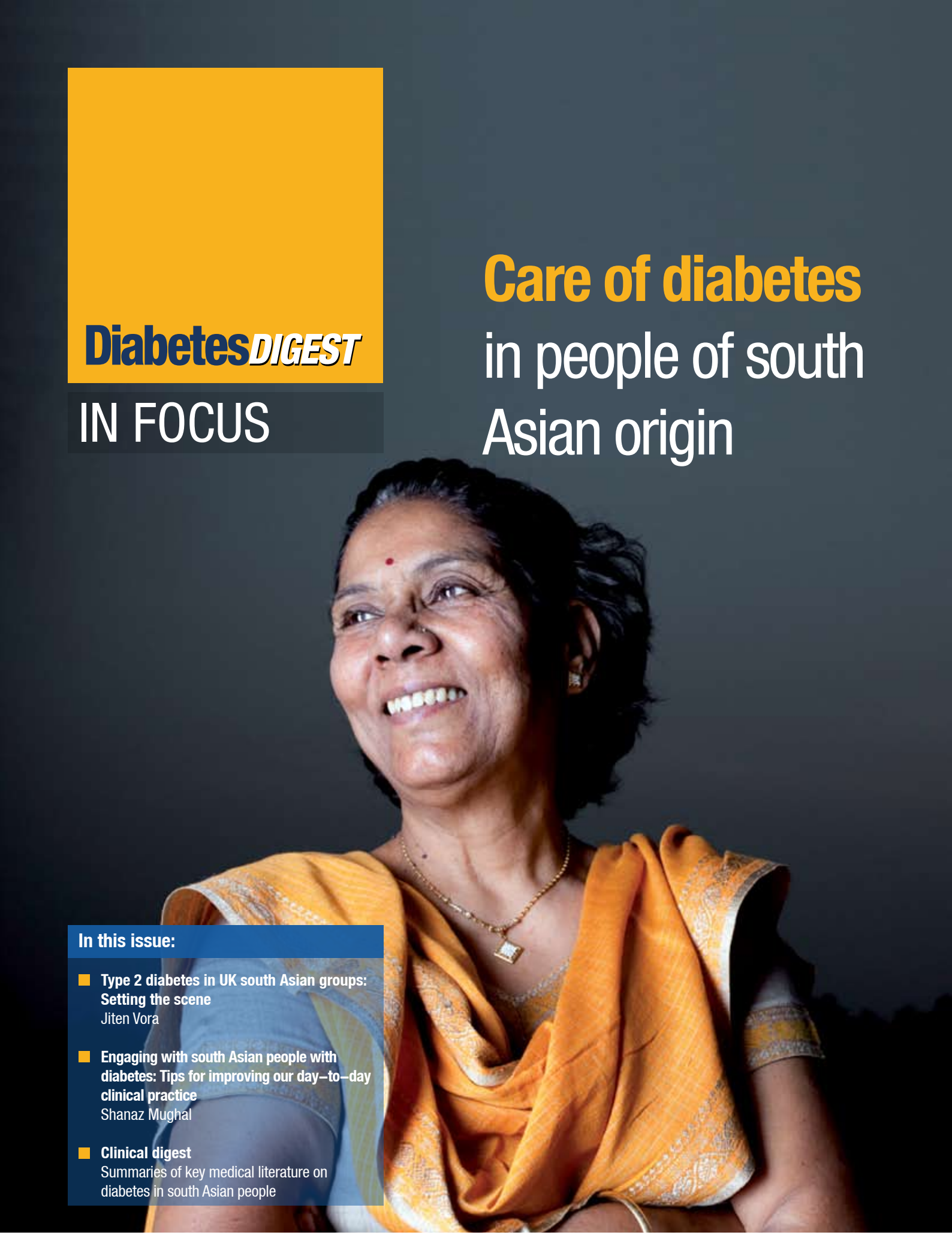
Diabetes DIGEST

IN FOCUS

Care of diabetes in people of south Asian origin



In this issue:

Sponsored supplement to *Diabetes Digest* Vol 9 No 2 2010.
Produced on behalf of Novartis Pharmaceuticals UK Ltd.

Prescribing information for Vildagliptin▼ and Vildagliptin/metformin▼ appears on page 8.

NOVARTIS

Type 2 diabetes in UK south Asian groups: Setting the scene

Aarabi M, Jackson PR (2005) *Eur J Cardiovasc Prev Rehabil* **12**: 46–51
Barnett AH et al (2006) *Diabetologia* **49**: 2234–46
Chandie Shaw PK et al (2006) *Diabetes Care* **29**: 1383–5
Chowdhury TA, Hitman GA (2007) *The British Journal of Diabetes & Vascular Disease* **7**: 279–82
Devendra D et al (2009) *Int J Clin Pract* **63**: 1446–50
Mather HM, Keen H (1985) *BMJ* **291**: 1081–4
Mather HM et al (1998) *Diabet Med* **15**: 53-9
Qiao Q et al (2003) *Diabetes Care* **26**: 1770–80
Raymond NT et al (2009) *Diabetes Care* **32**: 410–5
Saxena S et al (2004) *Arch Dis Child* **89**: 30–6
Whincup PH et al (2005) *Diabet Med* **22**: 1275–7

DECODA = Diabetes Epidemiology: Collaborative Analysis of Diagnostic Criteria in Asia
UKADS = UK Asian Diabetes Study

Jiten Vora is a Consultant Diabetologist, Liverpool

The DECODA study, which compared the prevalence of diabetes and impaired glucose tolerance in Asian countries, demonstrated that diabetes is particularly common in Indian populations – affecting approximately one in three of those studied who were aged between 50 and 59 (Qiao et al, 2003). While this demonstrates that diabetes is a significant problem within the south Asian peninsula, similar patterns have also been identified in the UK, where individuals of south Asian origin have been shown to be at a four-fold increased risk of developing type 2 diabetes compared with European comparators (Mather and Keen, 1985). Diabetes also presents approximately a decade earlier in south Asian people compared with comparator groups, both in UK and Asian studies (Mather and Keen, 1985; Qiao et al, 2003). Furthermore, cardiovascular complications are more common among those of south Asian origin and, in a key study by Mather et al (1998), cardiovascular mortality was two-fold increased in south Asian, as compared with European, people with diabetes.

Why is diabetes more common in south Asian groups?

There has been considerable debate as to why diabetes is more common in the south Asian population, and many hypotheses have been proposed. Genetic susceptibility to increasing insulin resistance has been suggested as one of the main factors (Choudhury and Hitman, 2007).

Indeed, UK data have demonstrated that young-to-adolescent boys and girls of south Asian origin are more likely to be obese or overweight than children in the general population (Saxena et al, 2004). Young UK south Asian individuals already demonstrate significant changes in their metabolic parameters, with higher insulin levels in the fasting state (Whincup et al, 2005).

Furthermore, south Asian people have comparatively sedentary lifestyles, and for a given BMI, demonstrate a higher percentage of body fat compared to European people as well as a propensity for central adiposity (Barnett et al, 2006). This increase in body fat, particularly abdominal fat, produces significant abnormal metabolic effects.

Management of diabetes in south Asian people

Current algorithms and pathways do not specifically identify the special needs of those with type 2 diabetes of south Asian origin. Likewise, many of the treatment targets suggested for people with type 2 diabetes are based on studies of Europid individuals, and there has been debate regarding risk calculation for cardiovascular outcomes in south Asian populations when using risk engines developed in other populations (Aarabi and Jackson, 2005).

As well as the increased cardiovascular risk and mortality, it is recognised from the UKADS and other studies that the prevalence of microvascular complications, such as retinopathy and nephropathy, is also increased (Chandie Shaw et al, 2006; Raymond et al, 2009). Thus, a more directed approach and guidelines specifically aimed at the management of type 2 diabetes in south Asian people are urgently required. These would ideally also take into consideration cultural differences, and would reflect specific management challenges, such as treatment changes during fasting for Ramadan, for which there are some supporting clinical trial data (such as those from Devendra et al, 2009).

Closing remarks

In this supplement, in keeping with the style of parent journal *Diabetes Digest*, we present easy-to-read, bullet-point summaries of some of the key trials that have informed our knowledge of diabetes in UK south Asian groups – be they related to epidemiology, cultural aspects or treatment adjustments during Ramadan, for example. Many of these have been referred to within this editorial and are worth studying in greater detail. Finally, Shanaz Mughal, a UKADS contributor, provides a short article covering simple, practical ways in which we, as healthcare professionals, can engage more successfully with people with diabetes who originate from south Asia. ■

Engaging with south Asian people with diabetes: Tips for improving our day–to–day clinical practice

Previous studies have suggested that UK south Asian people with diabetes have higher diastolic and systolic blood pressure, total cholesterol and HbA_{1c} levels than white European people (Raymond et al, 2009), and are less likely to achieve QOF indicators for those parameters (Gray et al, 2007).

While the imbalance in the prevalence and outcomes associated with diabetes between UK south Asian and other populations is likely to be multifactorial and to involve a genetic aspect, it is also probably partly due to cultural aspects, such as differences in access to NHS services and attitudes to medical treatment (Khunti et al, 2009).

Given the above, it is clear that there is a strong need for healthcare professionals to engage effectively with UK south Asian groups, ensuring that risk factor management is improved where possible. So, what practical steps can be taken to optimise our everyday clinical practice? The following are tips based on my own personal experience that may prove helpful in your own practice.

1. **Know the population you are serving.** South Asian people tend to congregate in tight-knit communities in boroughs. The following are helpful aspects to study in order to offer an appropriately tailored service in your locality.
   a. *Common names* (e.g. Bibi, Begum, Kaur, Singh). Noticing naming patterns will give you insight into groups who may have similar needs.
   b. *Religion.* Identifying a person's religion may provide useful insight into lifestyle and beliefs, for example.
   c. *Languages spoken and written.* Bear in mind that some south Asian languages or dialects that are spoken may not be written. For example, Mirpuri and Pushto are spoken-only, meaning that it is not possible to provide written educational materials (see point seven).
   d. *Dietary habits.* South Asian families may have distinct dietary habits – Bangladeshi men and women eat less fruit than those in other groups, for example (Hirani and Primatesta, 2001). Also, remember that the person with diabetes may not be the person within the household who does the cooking. From a social etiquette perspective, in UK Asian households guests may be encouraged to eat rich snacks, and refusing can be seen as embarrassing or impolite (Hawthorne et al, 1993).
   e. *Religious rituals.* In the case of Muslim people, fasting during Ramadan, or pilgrimage during Hajj will have implications for blood glucose-lowering medication. For example, this year Ramadan takes place between 11 August and 9 September, and it would be sensible to assess Muslim people wishing to fast in good time to discuss any necessary adjustments to the blood glucose lowering treatment regimen. In 2010, Hajj (pilgrimage to Mecca) takes place between 14 and 17 November, and the changes in diet and daily activity for those who attend will again possibly necessitate treatment adjustments and associated educational input from the healthcare team. (Readers should bear in mind that other religions also encompass rituals with implications for diabetes management.)
   f. *Smoking and exercise habits.* Bangladeshi men in particular are more likely to smoke or chew tobacco than men in the general population, for example (Boreham, 2001), and all south Asian groups engage in less physical activity than the general population (Fischbacher et al, 2004). Bear in mind, however, that some culturally sensitive exercise programmes – such as bhangra dancing – may already exist in the local area.

2. **Make use of Asian link workers** to:
   a. Work with the multidisciplinary team and to act as an advocate for the south Asian person with diabetes, translating where required.

Shanaz Mughal is Diabetes Specialist Nurse Coordinator, Birmingham

Right: The author (front) with her local Asian link workers.

b. Implement measures to encourage concordance with treatment (see point four).
c. Help with administration tasks.
d. Help with clinical assessments, provided that they are competent to do so.

3. **Ask south Asian patients to bring all their medications and blood glucose monitoring equipment to each consultation** with them and consider the steps below. In my experience, if you ask people to bring their medication and equipment but then do not refer to it during the consultation, they will not bring it to subsequent appointments.
   a. Do not assume that what is written in the notes or on the medication boxes or bottles is what is being taken.
   b. Check what is being said by counting tablets and referring back to prescriptions issued.
   c. Always ask the person with diabetes to relay back to you what you have asked of them to check understanding.

4. **Implement measures to encourage and assess concordance with pharmacotherapy.** South Asian people may be less concerned about adhering to their treatments than other groups (Khunti et al, 2009), and there may be myths and misconceptions to dispel. For example, research has suggested that some south Asian people consider their oral antidiabetes drugs to be for symptomatic benefit only (Lawton et al, 2005); others may believe that herbal remedies such as karela juice can cure diabetes (Hawthorne et al, 1993). Some suggestions to improve adherence are:
   a. Use south Asian link workers to help where you can.
   b. Use signs, symbols and stickers to signify medication timings and amounts.
   c. Use fixed-dose combination therapies where appropriate. For example, there are three such combination therapies for blood glucose lowering – metformin/pioglitazone, metformin/rosiglitazone and metformin/vildagliptin – and several for hypertension and lipid-lowering.

5. **Take into account that mealtimes may differ between south Asian and western societies.** For example, the main evening meal may be as late as 11 pm or midnight in some families or groups. Meal timings and patterns will also change during times of fasting, such as Ramadan, when there are two daily meals: Sehri (pre-dawn) and Iftar (after sunset). This has implications for the advice given regarding timing and dosing of blood glucose-lowering therapies and possibly also self-monitoring of blood glucose.

6. **Involve the extended family in consultations and education.** This may help others in the family to gain an understanding of diabetes, and may be helpful or necessary in families where there is a language barrier.

7. **Use audiovisual aids where appropriate.** While some south Asian people cannot read their own language, remember that other languages or dialects are not available in written form.

8. **Use blood glucose meters that do not require calibration, are simple to use and have a memory for obtaining results with a time and date.** This can be helpful when making decisions regarding blood glucose-lowering therapy.

9. **Telephoning patients 1–2 days before a scheduled appointment** can encourage attendance.

Conclusions

In summary, it is key that healthcare professionals offer a service to people with diabetes in UK south Asian groups that is culturally sensitive, taking into account customs, religious practices, lifestyle, food and language. There are a number of relatively simple, practical steps that can be implemented to improve success in everyday clinical practice. ■

Boreham R (2001) Use of tobacco products. *Health Survey for England – The Health of Minority Ethnic Groups '99.* DH, London

Fischbacher CM, Hunt S, Alexander L (2004) How physically active are South Asians in the United Kingdom? A literature review. *J Public Health (Oxf)* **26**: 250–8

Gray J, Millett C, Saxena S et al (2007) Ethnicity and quality of diabetes care in a health system with universal coverage: population-based cross-sectional survey in primary care. *J Gen Intern Med* **22**: 1317–20

Hawthorne K, Mello M, Tomlinson S (1993) Cultural and religious influences in diabetes care in Great Britain. *Diabet Med* **10**: 8–12

Hirani V, Primatesta P (2001). Eating habits. *Health Survey for England – The Health of Minority Ethnic Groups '99.* DH, London

Khunti K, Kumar S, Brodie J (2009) *Diabetes UK and South Asian Health Foundation recommendations on diabetes research priorities for British South Asians.* Diabetes UK, London

Lawton J, Ahmad N, Hallowell N et al (2005) Perceptions and experiences of taking oral hypoglycaemic agents among people of Pakistani and Indian origin: qualitative study. *BMJ* **330**: 1247

Raymond NT, Varadhan L, Reynold DR et al (2009) Higher prevalence of retinopathy in diabetic patients of South Asian ethnicity compared with white Europeans in the community: a cross-sectional study. *Diabetes Care* **32**: 410–5

Diabetes in south Asian people: epidemiology, risk factors, cultural issues and management

DIABETOLOGIA

Reviewing T2DM, CV risk in the UK south Asian population

1 A cluster of metabolic abnormalities, predictive of type 2 diabetes (T2DM) and cardiovascular (CV) disease, affect people of south Asian origin more frequently than people of European origin.

2 It has been suggested that some risk factors associated with T2DM in south Asian groups are enhanced by migration or urbanisation, and have contributed to the four- to six-fold increased risk of T2DM in the UK's south Asian population.

3 South Asian people present with T2DM at a significantly younger age than Europid people, placing them at particular risk of complications, known to increase with T2DM duration.

4 Coronary heart disease mortality rates are 50% higher among south Asian people than the total population rate of England and Wales, with their first myocardial infarction occurring approximately 5 years earlier.

5 BMI is an unreliable indicator in south Asian groups. The average BMI of UK south Asians is similar to that of the Europid population, but is confounded by increased deposition of metabolically active intra-abdominal fat, which is strongly related to insulin resistance.

6 Risk-reduction strategies, including screening and treatment for dyslipidaemia, hypertension and diabetes, do not adequately target people of south Asian origin in the UK.

7 A high proportion of avoidable morbidity in people of south Asian origin is associated with T2DM, CV disease and their complications. The authors suggest that this issue will grow in magnitude, as successive immigrant generations are also affected.

Barnett AH, Dixon AN, Bellary S et al (2006) Type 2 diabetes and cardiovascular risk in the UK south Asian community. *Diabetologia* **49**: 2234–46

> ***"Risk factors associated with type 2 diabetes in south Asian groups are enhanced by migration or urbanisation and have contributed to the four- to six-fold increased risk of type 2 diabetes in the UK's south Asian population."***

J GEN INTERN MED

South Asian people less likely to meet QOF targets

1 The authors investigated differences in clinical outcomes for diabetes between three ethnic groups in a UK population: black, south Asian, white.

2 Between November 2005 and January 2006, data from the electronic records of 32 primary care practices were collected.

3 Adults with diabetes (n=7605) registered at the participating practices were included and percentage achievement of Quality and Outcomes Framework (QOF) indicators stratified by ethnic group.

4 Variation in process measures of care were modest between the groups. No significant difference in recent measurement of clinical indicators between the groups was seen.

5 Black people and people of south Asian origin were found to meet all three QOF indicators for HbA_{1c} (≤7.4% [57 mmol/mol]), blood pressure (≤145/85 mmHg) and total cholesterol (≤5 mmol/L) significantly less than white people (adjusted odds ratio 0.76 for both black and south Asian people, compared with white people).

6 The authors suggest that while diabetes care was shown to be applied equitably, systematic successes in the process of care did not confer improvement in intermediate clinical outcomes equally, with black and south Asian people achieving poorer outcomes.

Gray J, Millett C, Saxena S et al (2007) Ethnicity and quality of diabetes care in a health system with universal coverage: population-based cross-sectional survey in primary care. *J Gen Intern Med* **22**: 1317–20

EUR J CARDIOVASC PREV REHABIL

Tool for predicting CHD risk in people of south Asian origin

1 To establish a simple method for coronary heart disease (CHD) risk prediction in people of south Asian origin, the authors adjusted the Framingham equation.

2 Risk factor data from 4497 individuals without cardiovascular disease who were included in the *Health Survey for England* (HSE) 1998 were employed to test adjustments to Framingham risk factor variables to allow for the increased CHD risk observed in south Asian people without diabetes.

3 The HSE 1999 dataset was used to assess the sensitivity and specificity of the above adjustments in south Asian people without diabetes. The different adjustments were compared using receiver-operating characteristic curves.

4 Multiplying the total:HDL-cholesterol ratio by 1.5 most accurately accounted for increased risk in south Asian people. For simplicity and acceptable accuracy, however, adding 10 years to the actual age of south Asian people was the best method of calculating CHD risk using the Framingham equation.

Aarabi M, Jackson PR (2005) Predicting coronary risk in UK south Asians: and adjustment method for Framingham-based tools. *Eur J Cardiovasc Prev Rehabil* **12**: 46–51.

"Ethnic differences in the efficacy and adverse effects of oral antidiabetes drugs should be studied, as well as the reluctance to initiate insulin therapy in the south Asian group."

DIABETES UK AND THE SOUTH ASIAN HEALTH FOUNDATION

Diabetes research priorities for UK south Asian people

1 The high prevalence, and associated increases in morbidity and mortality, of type 2 diabetes (T2DM) in British people of south Asian origin prompted Diabetes UK and the South Asian Health Foundation to produce recommendations for research on the condition as manifested in this group.

2 Sixteen areas for investigation were identified, including participation in research, epidemiology, diet and nutrition epidemiology, genetics, cultural aspects, screening, T2DM prevention and T2DM in children and adolescents.

3 The authors suggested that diabetes registries with ethnicity coding be established.

4 Qualitative studies to better understand cultural attitudes to diabetes were also called for.

5 Ethnic differences in the efficacy and adverse effects of oral antidiabetes drugs should be studied, as well as the reluctance to initiate insulin therapy in this group.

Khunti K, Kumar S, Brodie J (2009) *Diabetes UK and South Asian Health Foundation Recommendations on Diabetes Research Priorities for British South Asians.* Diabetes UK, London

"Small blood pressure benefits were achieved with the culturally tailored care package; however, generating improvements in glycaemic control remains a significant challenge."

DIABETES CARE

Diabetic retinopathy in UK south Asian and white European people with diabetes

1 In this sub-study of UKADS (UK Asian Diabetes Study), the investigators compared the prevalence of retinopathy and its associated risk factors in UK south Asian and white European groups.

2 A cross-sectional study encompassing 10 English general practices was performed. Overall 1035 people with type 2 diabetes were studied; approximately 41% were of south Asian ethnicity.

3 As well as grading of retinal photographs to assess the presence of diabetic retinopathy, sight-threatening retinopathy, maculopathy and previous laser therapy, data were collected regarding the following risk factors: age at diagnosis, duration and treatment of diabetes, HbA_{1c} level, cholesterol and blood pressure.

4 Those in the south Asian group had statistically significantly increased systolic (+7 mmHg) and diastolic (+10 mmHg) blood pressures, HbA_{1c} (+0.4% [+5 mmol/mol]) and total cholesterol levels (0.3 mmol/L) compared with the European comparator group (all $P<0.0001$).

5 The south Asian group were diagnosed with diabetes earlier than the white European participants (53.0 years vs. 58.6 years; $P<0.0001$) and had a shorter duration of diabetes (7.6 vs. 8.8 years; $P<0.0001$)

6 The risk of developing any retinopathy and maculopathy were significantly elevated in the south Asian group, after adjusting for potential confounding variables.

7 To rectify this inequality, the authors concluded that the first step is to make healthcare professionals aware that south Asian people are at increased risk of visual impairment or blindness.

Raymond NT, Varadhan L, Reynold DR et al (2009) Higher prevalence of retinopathy in diabetic patients of South Asian ethnicity compared with white Europeans in the community: a cross-sectional study. *Diabetes Care* **32**: 410–5

LANCET

Culturally tailored diabetes care for UK south Asian people

1 The effectiveness of a culturally sensitive, enhanced care package for type 2 diabetes and cardiovascular risk factors in people of south Asian origin was investigated.

2 Twenty-one UK general practices were randomised to implement an enhanced care intervention (nine practices; $n=868$) or standard care (12 practices; $n=618$).

3 The intervention group received additional time with a practice nurse and support from a link worker and a diabetes specialist nurse. All practices were provided with clear clinical targets and prescribing algorithms.

4 During the 2-year study, the whole study population achieved significant decreases in systolic (4.9 mmHg; 95% confidence interval [CI] 4.0–5.9 mmHg) and diastolic blood pressure (BP; 3.8 mmHg; 95% CI 3.2–4.4 mmHg) and cholesterol (0.45 mmol/L; 95% CI 0.40 to 0.51 mmol/L), respectively). A non-significant increase in population HbA_{1c} (0.04%; 95% CI –0.04% to 0.13%; $P=0.290$) was also observed.

5 In the intervention group, diastolic BP was significantly improved (by 1.91 mmHg; 95% CI –2.88 to –0.94 mmHg; $P=0.0001$), as was mean arterial pressure (by 1.36 mmHg; 95% CI –2.49 to –0.23 mmHg; $P=0.0180$). Between-group differences for total cholesterol, systolic BP and HbA_{1c} were not significant.

6 Small BP benefits were achieved with the culturally tailored care package; however, generating improvements in glycaemic control remains a significant challenge.

Bellary S, O'Hare JP, Raymond NT et al (2008) Enhanced diabetes care to patients of south Asian ethnic origin (the United Kingdom Asian Diabetes Study): a cluster randomised controlled trial. *Lancet* **371**: 1769–76

DIABETES CARE

Management of diabetes during Ramadan: ADA recommendations

1 The current authors convened to develop an American Diabetes Association (ADA) consensus statement on the medical management of people with diabetes who fast during Ramadan.

2 Major risks for the person with diabetes when fasting are hypo- and hyperglycaemia, diabetic ketoacidosis, dehydration and thrombosis.

3 Ramadan management plans should be individualised, with frequent self-monitoring of blood glucose (BG) levels during the fast being essential. Nutritional advice should be aimed at maintaining a constant body mass.

4 For those wishing to fast during Ramadan, preparation should include a medical assessment 1–2 months before fasting, along with educational counselling concerning topics such as self-care, hypo- and hyperglycaemia.

5 The fast must be broken if: (i) BG is at any time <3.3 mmol/L; (ii) BG is <3.9 mmol/L in the first few hours of the fast; (iii) BG is >16.7 mmol/L.

6 For people with type 2 diabetes, sulphonylureas were believed by the authors to be unsuitable for use during fasting due to risk of hypoglycaemia.

7 For insulin-dependent people, the main goal of Ramadan therapy should be to maintain appropriate basal insulin supply.

Al-Arouj M, Bouguerra R, Buse J et al (2005) Recommendations for management of diabetes during Ramadan. *Diabetes Care* **28**: 2305–11.

"For those wishing to fast during Ramadan, preparation should include a medical assessment 1–2 months before fasting, along with educational counselling concerning topics such as self-care, hypo- and hyperglycaemia."

BMJ

South Asian attitudes to oral antidiabetes drugs

1 The current authors conducted a cross-sectional survey in Edinburgh of 32 people with type 2 diabetes of Pakistani or Indian origin.

2 The respondents had "complex and ambivalent" views about oral antidiabetes drugs (OADs).

3 Because the participants considered UK healthcare professionals to be trustworthy and competent, they considered OADs to be an important element of their treatment regimen.

4 However, less than half of respondents reported taking the tablets as directed. Overall, 15 respondents volunteered deliberately attempting to reduce OAD intake.

5 Reasons given included belief that OADs were for symptom relief only, and that they could have adverse health effects in the long term.

Lawton J, Ahmad N, Hallowell N et al (2005) Perceptions and experiences of taking oral hypoglycaemic agents among people of Pakistani and Indian origin: qualitative study. *BMJ* **330**: 1247

INT J CLIN PRACT

Vildagliptin versus gliclazide during Ramadan fasting

1 The impact of fasting during Ramadan on the management of diabetes is not fully understood, though an increased risk of severe hypoglycaemic events has been reported.

2 The authors sought to compare the incidence of hypoglycaemic events, weight change and HbA_{1c} before and after Ramadan in a group of Muslim people with type 2 diabetes treated with metformin plus either gliclazide or vildagliptin.

3 Participants (n=52) were recruited from primary care practices in northwest London. Inclusion criteria were an HbA_{1c} >8.5% (>69 mmol/mol) despite treatment with metformin 2 g daily. They were given either gliclazide (up to 160 mg twice daily; n=26) or vildagliptin (50 mg twice daily; n=26).

4 Two weeks prior to, and 10 days following Ramadan, participant data on hypoglycaemic events, HbA_{1c} and weight were recorded. Education on recognising and managing hypoglycaemia was provided prior to Ramadan.

5 Blood glucose diaries and blood glucose meters were analysed for episodes of hypoglycaemia. Hypoglycaemia was defined as a blood glucose level <3.5 mmol/L, with or without symptoms.

6 During Ramadan, at least one hypoglycaemic event was recorded in two people in the vildagliptin arm (7.7%), compared with 16 in the gliclazide arm (61.5%; P<0.001).

7 Compared with before Ramadan, the mean number of hypoglycaemic events was significantly reduced in the vildagliptin arm at the end of Ramadan, but was increased in the gliclazide arm (P<0.0168 for between-group difference in the change in frequency).

8 Both arms achieved similar reductions in HbA_{1c} (of approximately 1.2% [13 mmol/mol]) during Ramadan and non-significant increases in weight.

9 It was concluded that adding vildagliptin to metformin monotherapy for Ramadan was associated with a reduction in the incidence of hypoglycaemia.

Devendra D, Gohel B, Bravis V et al (2009) Vildagliptin therapy and hypoglycaemia in Muslim type 2 diabetes patients during Ramadan. *Int J Clin Pract* **63**: 1446–50

"Adding vildagliptin to metformin monotherapy for Ramadan was associated with a reduction in the incidence of hypoglycaemia."

Vildagliptin ▼
UK ABBREVIATED PRESCRIBING INFORMATION

Presentation: Tablets containing 50mg vildagliptin. Indications: Treatment of type 2 diabetes mellitus as dual oral therapy in combination with: metformin, in patients with insufficient glycaemic control despite maximal tolerated dose of metformin monotherapy; a sulphonylurea, in patients with insufficient glycaemic control despite maximal tolerated dose of a sulphonylurea and for whom metformin is inappropriate due to contraindications or intolerance; a thiazolidinedione, in patients with insufficient glycaemic control and for whom the use of a thiazolidinedione is appropriate. **Dosage**: 50mg twice daily (morning and evening) when used in dual combination with metformin or a thiazolidinedione; 50mg once daily in the morning when used in dual combination with a sulphonylurea. Vildagliptin may be taken with or without a meal. No dosage adjustment is required in the elderly, or in patients with mild renal impairment. Vildagliptin is not recommended in moderate to severe renal impairment or hepatic impairment including patients with pre-treatment ALT or AST > 3x ULN. Vildagliptin is not recommended for use in children and adolescents. **Contra-indications**: Hypersensitivity to the active substance or to any of the excipients. **Precautions**: Caution should be exercised in patients aged 75 years and older due to limited clinical experience. Vildagliptin is not a substitute for insulin in insulin-requiring patients. Vildagliptin should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis. Due to limited experience, Vildagliptin is not recommended in patients with moderate to severe renal impairment or in patients with ESRD on haemodialysis. It is recommended that LFTs are monitored prior to initiation of Vildagliptin, at three-monthly intervals in the first year and periodically thereafter. If transaminase levels are increased, patients should be monitored with a second liver function evaluation to confirm the finding and be followed thereafter with frequent liver function tests until the abnormality(ies) return(s) to normal. If AST or ALT persist at 3x ULN, Vildagliptin treatment should be stopped. Patients who develop jaundice or other signs of liver dysfunction should discontinue Vildagliptin. Following withdrawal of treatment with Vildagliptin and LFT normalisation, treatment with Vildagliptin should not be reinitiated. Due to limited clinical experience, use with caution in patients with congestive heart failure of NYHA functional class I–II, and do not use in patients with NYHA functional class III IV. In keeping with routine care of the diabetic patient, monitoring for skin disorders, such as blistering or ulceration, is recommended. The tablets contain lactose; patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicinal product. Vildagliptin should not be used in pregnancy or lactation. Patients who experience dizziness as a side effect should avoid driving vehicles or using machines. **Drug interactions**: Vildagliptin has a low potential for interactions with co-administered medicinal products, including drugs that are substrates, inhibitors or inducers of CYP450 enzymes. In pharmacokinetic studies, no interactions were seen with pioglitazone, metformin, glibenclamide, digoxin, warfarin, amlodipine, ramipril, valsartan or simvastatin. As with other oral antidiabetes medicinal products, the glucose-lowering effect of Vildagliptin may be reduced by certain active substances, including thiazides, corticosteroids, thyroid products and sympathomimetics. **Pregnancy and Lactation**: There are no adequate data on the use of Vildagliptin in pregnant women, hence the potential risk for humans is unknown. Due to lack of data, Vildagliptin should not be used during pregnancy. Animal studies have shown excretion of Vildagliptin in milk; it is not know whether this is the case in humans, therefore Vildagliptin should not be used during lactation. **Side-effects**: The majority of adverse reactions were mild and transient, not requiring treatment discontinuation. General: rare cases of hepatic dysfunction (including hepatitis). ALT or AST elevations ≥3xULN for Vildagliptin 50mg od (0.2%), Vildagliptin 50mg bd (0.3%) compared to 0.2% with comparators in clinical trials. Rare cases of angioedema at similar rates to controls. Combination with metformin *common*: tremor, headache, dizziness, nausea, hypoglycaemia; *uncommon*: fatigue. Clinical trials of up to and more than 2 years duration did not show any additional safety signals or unforeseen risks when Vildagliptin was added on to metformin. Combination with a sulphonlyurea *common*: tremor, headache, dizziness, asthenia, hypoglycaemia; *uncommon*: constipation; *very rare*: nasopharyngitis; Combination with a thiazolidinedione *common*: weight increase, peripheral oedema; *uncommon*: headache, asthenia, hypoglycaemia. Monotherapy *Common*: dizziness; *uncommon*: headache, peripheral oedema, constipation, arthralgia, hypoglycaemia. *Very rare*: upper respiratory tract infection, nasopharyngitis. Post-marketing experience: urticaria (frequency not known). **Legal Category**: POM **Packs**: Vildagliptin (Galvus®) 50mg tablets (EU/1/07/414/001-010), £31.76 per pack of 56 tablets. ® denotes registered trademark. Marketing Authorisation Holder: Novartis Europharm Limited, Wimblehurst Road, Horsham, West Sussex, RH12 5AB. Full prescribing information is available on request from Novartis Pharmaceuticals UK Ltd., Frimley Business Park, Frimley, Camberley, Surrey GU16 7SR. Telephone (01276) 698370; Fax (01276) 698449. **Date of preparation**: September 2009.

Vildagliptin/metformin Tablets ▼
UK ABBREVIATED PRESCRIBING INFORMATION

Presentation: Tablets containing 50mg Vildagliptin and 850mg metformin or 50mg Vildagliptin and 1000mg metformin. **Indications**: Type 2 diabetes mellitus in patients who are unable to achieve sufficient glycaemic control at their maximally tolerated dose of oral metformin alone or who are already treated with the combination of Vildagliptin and metformin as separate tablets. **Dosage**: Initiate at 50mg/850mg bd or 50mg/1000mg bd (morning and evening) based on patient's current dose of metformin. Dosing with or just after food may reduce gastrointestinal symptoms associated with metformin. There is no clinical experience of Vildagliptin and metformin in combination with other antidiabetes agents. Vildagliptin/metformin tablets are not recommended in patients aged >75yrs or in patients <18yrs due to lack of data on safety and efficacy in these groups. **Contra-indications**: Hypersensitivity to the active substance or to any of the excipients; renal failure/dysfunction (CrCl <60 ml/min); acute conditions with potential to alter renal function (e.g. dehydration, severe infection, shock, i.v. administration of iodinated contrast agents); acute or chronic disease which may cause tissue hypoxia (e.g. cardiac or respiratory failure, recent MI, shock); hepatic impairment, including patients with pre-treatment AST or ALT >3xULN; acute alcohol intoxication, alcoholism; lactation. **Precautions**: Vildagliptin/metformin tablets should not be used in patients with type 1 diabetes. Lactic acidosis (characterized by acidotic dyspnoea, abdominal pain, hypothermia, coma, decreased blood pH, plasma lactate levels >5mmol/l, increased anion gap and lactate/pyruvate ratio) can occur due to metformin accumulation (e.g. in significant renal failure, hepatic impairment). Other risk factors for lactic acidosis should be assessed (e.g. poorly controlled diabetes, ketosis, prolonged fasting, excessive alcohol intake, conditions associated with hypoxia). If metabolic acidosis is suspected, treatment should be discontinued and the patient hospitalised immediately. Serum creatinine should be monitored at least once a year in patients with normal renal function and 2–4 times a year in patients with serum creatinine levels at the upper limit of normal and in elderly patients. Special caution should be exercised in elderly patients where renal function may become impaired (e.g. when initiating antihypertensives, diuretics or NSAIDs). It is recommended that LFTs are monitored prior to initiation of Vildagliptin/metformin tablets, at three-monthly intervals in the first year and periodically thereafter. If transaminase levels are increased, patients should be monitored with a second liver function evaluation to confirm the finding and be followed thereafter with frequent liver function tests until the abnormality(ies) return(s) to normal. If AST or ALT persist at 3x ULN, Vildagliptin/metformin tablets should be stopped. Patients who develop jaundice or other signs of liver dysfunction should discontinue Vildagliptin/metformin. Following withdrawal of treatment with Vildagliptin/metformin and LFT normalisation, treatment with Vildagliptin/metformin should not be reinitiated. In keeping with routine care of the diabetic patient, monitoring for skin disorders, such as blistering or ulceration, is recommended. Vildagliptin/metformin tablets should be discontinued 48 hours before elective surgery with general anaesthesia and should not usually be resumed earlier than 48 hours afterwards. Vildagliptin/metformin should be discontinued prior to, or at the time of, the administration of iodinated contrast agent and not reinstituted until 48 hours afterwards, and only after renal function has been re-evaluated and found to be normal. Patients who experience dizziness as a side effect should avoid driving vehicles or using machines. **Drug interactions**: Vildagliptin has a low potential for interactions with co-administered medicinal products, including drugs that are substrates, inhibitors or inducers of CYP450 enzymes. In pharmacokinetic studies, no interactions were seen with pioglitazone, metformin, glibenclamide, digoxin, warfarin, amlodipine, ramipril, valsartan or simvastatin. As with other oral antidiabetes medicinal products the glucose-lowering effect of Vildagliptin may be reduced by certain active substances, including thiazides, corticosteroids, thyroid products and sympathomimetics. Close monitoring of glycaemic control, dose adjustment within the recommended posology and changes in diabetic treatment should be considered when cationic medicinal products that are eliminated by renal tubular secretion (e.g. cimetidine) are co-administered. Glucocorticoids, beta-2-agonists, diuretics and ACE inhibitors may alter blood glucose. The patient should be informed and more frequent blood glucose monitoring performed, especially at the beginning of treatment. If necessary, the dosage of Vildagliptin/metformin tablets may need to be adjusted during concomitant therapy and on its discontinuation. **Pregnancy and Lactation**: There are no adequate data on the use of Vildagliptin/metformin in pregnant women, hence the potential risk for humans is unknown. Due to lack of data, Vildagliptin/metformin should not be used during pregnancy. It is not known whether Vildagliptin is excreted in human milk, but metformin is known to in small amounts. Due to lack of human data, Vildagliptin/metformin should not be used during lactation. **Side-effects**: The majority of adverse reactions were mild and transient, not requiring treatment discontinuations. General (Vildagliptin): rare cases of hepatic dysfunction (including hepatitis). ALT or AST elevations ≥3xULN for vildagliptin 50mg od (0.2%), Vildagliptin 50mg bd (0.3%) compared to 0.2% with comparators in clinical trials. Rare cases of angioedema at similar rates to controls. Vildagliptin and metformin in combination *common*: tremor, headache, dizziness, nausea, hypoglycaemia; *uncommon*: fatigue. Clinical trials of up to and more than 2 years' duration did not show any additional safety signals or unforeseen risks when Vildagliptin was added on to metformin. Vildagliptin monotherapy *common*: dizziness; *uncommon*: headache, constipation, arthralgia, peripheral oedema, hypoglycaemia; *very rare*: upper respiratory tract infection, nasopharyngitis. Post-marketing experience: urticaria (frequency not known). Metformin *very common*: Nausea, vomiting, diarrhoea, abdominal pain and loss of appetite; *common*: metallic taste; *very rare*: LFT abnormalities or hepatitis, decrease of vitamin B12 absorption and lactic acidosis, skin reactions such as erythema, pruritis and urticaria. **Legal Category**: POM **Packs**: Vildagliptin/metformin (Eucreas®) 50mg/850mg tablets (EU/1/07/425/003), £31.76 per pack of 60 tablets; Vildagliptin/metformin (Eucreas®) 50mg/1000mg tablets (EU/1/07/425/009), £31.76 per pack of 60 tablets. ® denotes registered trademark. Marketing Authorisation Holder: Novartis Europharm Limited, Wimblehurst Road, Horsham, West Sussex, RH12 5AB. Full prescribing information is available on request from Novartis Pharmaceuticals UK Ltd., Frimley Business Park, Frimley, Camberley, Surrey GU16 7SR. Telephone (01276) 698370; Fax (01276) 698449. **Date of preparation**: September 2009.

Adverse events should be reported. Reporting forms and information can be found at www.yellowcard.gov.uk. Adverse events should also be reported to Novartis Pharmaceuticals UK Ltd; please call (01276) 698370.

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SB Communications Group, 3.05 Enterprise House, 1–2 Hatfields, London, SE1 9PG. Tel: +44 (0)20 7627 1510. Fax: +44 (0)20 7627 1570.
Email: editorial@sbcommunicationsgroup.com. Web: www.sbcommunicationsgroup.com.