Diabetes in Shift Workers

Hamish Courtney
Diabetes Dept
Royal Victoria Hospital
Belfast
Tips for Married Shiftworkers

Don’t work shiftwork!

An update of an old saying about marriage might be: “Behind every great shiftworker stands a heroic spouse who understands the demands of the job.”

If you’re married, how well your partner copes with your work schedule is as important as how well you handle it. Here are some ideas to help you and your spouse successfully juggle the often competing demands of night work and marriage.

Take advantage of the good aspects to your schedule. There likely will be times when you’re working on a Friday or a Saturday night, when it
CAREERS FOR DIABETIC GIRLS IN NURSING

SIR,—My attention was drawn to the difficulty a teenage diabetic girl had experienced in gaining acceptance by schools of nursing. She was told that, although her examination grades were satisfactory, being diabetic made her an unsuitable candidate for nursing. In the belief that nursing was a particularly suitable career for a girl with diabetes, I made a survey of schools of nursing asking about their attitude towards admitting girls with diabetes. The result of this survey is set out below.

I wrote to the health authorities in England and all replied. The hospitals varied in size and types; some were independent and some were specialist. The addresses I obtained from the Direct 111 had necessitated their inspection. As far as I could ascertain, that the complacency during periods of mandatory night duty were assured of medical surveillance, in case of the sometimes inevitable physiological adjustment which must take place. The letter continues, "The nursing profession is supposed to be one of the caring professions, and if we cannot offer our resident expertise to help persons with such well-understood conditions as diabetes to gain satisfaction in a career of their choice then it is time to overhaul our ideas." Thirty-four other hospitals had strong reservations, suggesting that students try other jobs first. They pointed out the heavy physical demands, the longer working day, and the difficulty of adjustment to night shift. It was stated that pupils could be trained if the hospital was near their home or if they lived at home. However, they were willing to consider applications.

There was no correlation between the rejections and the size, type, or area of the hospital. They seemed quite unrelated in any way, with the exception of two which were specialised hospitals. Twelve hospitals stated that they would automatically reject all applications from diabetics; most of them gave no explanation, just straight refusals. Two, however, gave the reasons that the student nurses were too busy and often under considerable pressure. One hospital went on to say that, although on the whole candidates with diabetes mellitus would not be accepted, they had accepted student nurses with diabetes insipidus—usually after a head injury—and that they had been able to cope well.

Many of the letters showed a keen interest in the survey and pointed out how they had successfully trained pupils with diabetes. One hospital had trained a young man with severe diabetes who was now training to be a registered mental nurse at a psychiatric training school. It was made clear, however, by some hospitals that they had tried unsuccessfully to train pupils to become nurses—"the pressure had been too great for them."

It seems extraordinary that there should be being diabetic made her an unsuitable candidate for nursing.

ELLEN BAGSHAW
Lackmead School,
Ablington, Oxon OX14 1RF

SPRING HYPOGLYCAEMIA IN DIABETIC CHILDREN

SIR,—We have recently experienced an outbreak of serious hypoglycaemia among the children attending the Oxford paediatric diabetic clinic. It is generally recognised that with the longer hours of daylight diabetic children may require less insulin or more food in the spring, possibly related to more outdoor exercise. In our experience this usually occurs in April or May and the children and their families adapt their diabetic management without undue difficulty. This March, following a mild but dull winter, and before the weather had improved enough to encourage increased outdoor activities, we appear to have experienced the worst outbreak of hypo-
1529 Belgian workers followed for median 6.6 yrs
309 (20%) were regular shift workers

Metabolic syndrome OR 1.77 (95%CI 1.34-2.32)
<table>
<thead>
<tr>
<th>Age at baseline</th>
<th>Years of rotating shift work</th>
<th>N</th>
<th>OR (95% CI)&lt;sup&gt;a&lt;/sup&gt;</th>
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</thead>
<tbody>
<tr>
<td>&lt;45 years</td>
<td>Never</td>
<td>728</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>&lt;10 years</td>
<td>29</td>
<td>0.97 (0.36–2.59)</td>
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<tr>
<td></td>
<td>≥10 years</td>
<td>67</td>
<td>1.61 (0.90–2.84)</td>
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<td></td>
<td></td>
<td></td>
<td>*P = 0.11&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>≥45 years</td>
<td>Never</td>
<td>492</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>&lt;20 years</td>
<td>66</td>
<td>1.36 (0.75–2.49)</td>
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<tr>
<td></td>
<td>≥20 years</td>
<td>139</td>
<td>1.82 (1.23–2.69)</td>
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<td></td>
<td></td>
<td></td>
<td>*P = 0.003&lt;sup&gt;b&lt;/sup&gt;</td>
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</table>

<sup>a</sup> Age-adjusted.

<sup>b</sup> Significance of linear trend.
<table>
<thead>
<tr>
<th>Component</th>
<th>OR (95% CI)</th>
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<tbody>
<tr>
<td>Waist circumference $\geq 94$ cm</td>
<td>1.12 (0.88–1.42)</td>
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<tr>
<td>SBP/DBP $\geq 130/85$ mmHg and/or antihypertensive medication</td>
<td>1.31 (1.04–1.66)</td>
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<tr>
<td>HDL cholesterol $&lt; 40$ mg/dl</td>
<td>1.42 (1.02–1.99)</td>
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<tr>
<td>Triglycerides $\geq 220$ mg/dl</td>
<td>1.53 (1.22–1.92)</td>
</tr>
<tr>
<td>Non-fasting glucose $\geq 120$ mg/dl or diabetes type II</td>
<td>1.56 (1.18–2.05)</td>
</tr>
</tbody>
</table>

*Adjusted for age, waist circumference, diastolic blood pressure and HDL cholesterol at the initial examination.*
Shift work

Metabolic syndrome

???
Rotating Night Shift Work and Risk of Type 2 Diabetes: Two Prospective Cohort Studies in Women

An Pan¹, Eva S. Schernhammer²,³, Qi Sun¹,³, Frank B. Hu¹,²,³*

¹ Department of Nutrition, Harvard School of Public Health, Boston, Massachusetts, United States of America, ² Department of Epidemiology, Harvard School of Public Health, Boston, Massachusetts, United States of America, ³ Channing Laboratory, Department of Medicine, Brigham and Women’s Hospital and Harvard Medical School, Boston, Massachusetts, United States of America

Abstract

Background: Rotating night shift work disrupts circadian rhythms and has been associated with obesity, metabolic syndrome, and glucose dysregulation. However, its association with type 2 diabetes remains unclear. Therefore, we aimed to evaluate this association in two cohorts of US women.

Methods and Findings: We followed 69,269 women aged 42–57 in Nurses’ Health Study I (NHS I, 1988–2008), and 107,915 women aged 25–42 in NHS II (1989–2007) without diabetes, cardiovascular disease, and cancer at baseline. Participants were asked how long they had worked rotating night shifts (defined as at least three nights/month in addition to days and evenings in that month) at baseline. This information was updated every 2–4 years in NHS II. Self-reported type 2 diabetes was confirmed by a validated supplementary questionnaire. We documented 6,165 (NHS I) and 3,961 (NHS II) incident type 2 diabetes cases during the 18–20 years of follow-up. In the Cox proportional models adjusted for diabetes risk factors, duration of shift work was monotonically associated with an increased risk of type 2 diabetes in both cohorts. Compared with women who reported no shift work, the pooled hazard ratios (95% confidence intervals) for participants with 1–2, 3–9, 10–19, and ≥20 years of shift work were 1.05 (1.00–1.11), 1.20 (1.14–1.26), 1.40 (1.30–1.51), and 1.58 (1.43–1.74, p-value for trend <0.001), respectively. Further adjustment for updated body mass index attenuated the association, and the pooled hazard ratios were 1.03 (0.98–1.08), 1.06 (1.01–1.11), 1.10 (1.02–1.18), and 1.24 (1.13–1.37, p-value for trend <0.001).

Conclusions: Our results suggest that an extended period of rotating night shift work is associated with a modestly increased risk of type 2 diabetes in women, which appears to be partly mediated through body weight. Proper screening and intervention strategies in rotating night shift workers are needed for prevention of diabetes.

Please see later in the article for the Editors’ Summary.
Diabetes risk

- No shift work 1.00
- 2yr shift work 1.05 (1.0-1.11)
- 20yr shift work 1.58 (1.43-1.74)

Pan et al, PLoS Medicine 2011;8:e1001141
Shift work and vascular events: systematic review and meta-analysis

Manav V Vyas graduate student, Amit X Garg professor, Arthur V Iansavichus information specialist, John Costella research and instructional librarian, Allan Donner professor, Lars E Laugsand PhD candidate, Imre Janszky researcher, Marko Mrkobrada assistant professor, Grace Parraga associate professor, Daniel G Hackam associate professor

1Department of Epidemiology and Biostatistics, Western University, London, ON, Canada; 2Department of Medicine, Western University; 3Kidney Clinical Research Unit, Lawson Research Institute, London, ON, Canada; 4Research and Instructional Services, Allan and Betty Taylor Library, Western University; 5Clinical Trials Unit, Robarts Research Institute, Western University; 6Department of Public Health, Norwegian University of Science and Technology, Trondheim, Norway; 7Department of Public Health, Karolinska Institute, Stockholm, Sweden; 8Imaging Research Laboratories, Robarts Research Institute and Department of Medical Biophysics, Western University
<table>
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<th>Study</th>
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<th>P value</th>
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<th>Risk ratio (95% CI)</th>
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<td><strong>Case control studies</strong></td>
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<td>Babisch et al</td>
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<td>1.03 (0.80 to 1.33)</td>
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<td><strong>Total</strong></td>
<td>2.01</td>
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<td>Tuchsen et al 2006</td>
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<td>Yerlin</td>
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<td>Laugesen et al</td>
<td>3.28</td>
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<tr>
<td><strong>Total</strong></td>
<td>2.58</td>
<td>0.01</td>
<td>1.32 (1.07 to 1.63)</td>
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<td><strong>Retrospective cohort studies</strong></td>
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<td>Alfredsson et al</td>
<td>3.95</td>
<td>0.00</td>
<td>1.20 (1.09 to 1.31)</td>
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<td>Biggi et al</td>
<td>0.90</td>
<td>0.37</td>
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<td>Ellingsen et al</td>
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<td>1.99 (1.23 to 3.22)</td>
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<td>Haupt et al</td>
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<td>0.02</td>
<td>1.53 (1.06 to 2.21)</td>
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<td>Karlsson et al</td>
<td>1.30</td>
<td>0.19</td>
<td>1.11 (0.95 to 1.30)</td>
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<td>Koller</td>
<td>1.13</td>
<td>0.26</td>
<td>5.17 (0.30 to 89.43)</td>
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<td>Rafnsson and Gunnarsdottir</td>
<td>0.76</td>
<td>0.45</td>
<td>1.21 (0.74 to 1.98)</td>
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<tr>
<td>Taylor and Pocock</td>
<td>0.43</td>
<td>0.66</td>
<td>1.03 (0.90 to 1.18)</td>
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<tr>
<td><strong>Total</strong></td>
<td>2.84</td>
<td>0.00</td>
<td>1.19 (1.06 to 1.34)</td>
<td></td>
</tr>
</tbody>
</table>
Shift work

? 

Insulin resistance
Type 2 diabetes
Early report

Impact of sleep debt on metabolic and endocrine function

Karine Spiegel, Rachel Leproult, Eve Van Cauter

11 young males
One week of 4h sleep per night
One week of 12h sleep per night
Figure 2: Mean (SE) profiles of blood glucose and serum insulin during intravenous glucose tolerance test, and glucose and insulin responses to breakfast
Sleep Restriction for 1 Week Reduces Insulin Sensitivity in Healthy Men

Orfeu M. Buxton,¹,² Milena Pavlova,²,³ Emily W. Reid,¹ Wei Wang,¹,² Donald C. Simonson,¹,² and Gall K. Adler¹,²
FIG. 1. Protocol schema. (See research design and methods for a detailed description.)
G

![Graph showing insulin sensitivity (S_i) for sleep replete (10 hrs) and sleep restricted (5 hrs).](image)

Insulin sensitivity
\[S_i, \text{mU/L} \text{min}^{-1}\]

*\(p < 0.05\) for sleep replete vs. sleep restricted.

I

![Graph showing insulin sensitivity (M, mg/kg/min) for sleep replete (10 hrs) and sleep restricted (5 hrs).](image)

Insulin sensitivity
\[M, \text{mg/kg/min}\]

*\(p < 0.05\) for sleep replete vs. sleep restricted.
Shift work

Sleep disturbance

Insulin resistance
Type 2 diabetes
Association of Sleep Time With Diabetes Mellitus and Impaired Glucose Tolerance

Daniel J. Gottlieb, MD, MPH; Naresh M. Punjabi, MD, PhD; Ann B. Newman, MD, MPH; Helaine E. Resnick, PhD; Susan Redline, MD, MPH; Carol M. Baldwin, RN, PhD; F. Javier Nieto, MD, PhD

Background: Experimental sleep restriction causes impaired glucose tolerance (IGT); however, little is known about the metabolic effects of habitual sleep restriction. We assessed the cross-sectional relation of usual sleep time to diabetes mellitus (DM) and IGT among participants in the Sleep Heart Health Study, a community-based prospective study of the cardiovascular consequences of sleep-disordered breathing.

Methods: Participants were 722 men and 764 women, aged 53 to 93 years. Usual sleep time was obtained by standardized questionnaire. Diabetes mellitus was defined as a serum glucose level of 126 mg/dL or more (≥7.0 mmol/L) fasting or 200 mg/dL or more (≥11.1 mmol/L) 2 hours following standard oral glucose challenge or medication use for DM. Impaired glucose tolerance was defined as a 2-hour postchallenge glucose level of 140 mg/dL or more (≥7.8 mmol/L) and less than 200 mg/dL. The relation of sleep time to DM and IGT was examined using categorical logistic regression with adjustment for age, sex, race, body habitus, and apnea-hypopnea index.

Results: The median sleep time was 7 hours per night, with 27.1% of subjects sleeping 6 hours or less per night. Compared with those sleeping 7 to 8 hours per night, subjects sleeping 5 hours or less and 6 hours per night had adjusted odds ratios for DM of 2.51 (95% confidence interval, 1.57-4.02) and 1.66 (95% confidence interval, 1.15-2.39), respectively. Adjusted odds ratios for IGT were 1.33 (95% confidence interval, 0.83-2.15) and 1.58 (95% confidence interval, 1.15-2.18), respectively. Subjects sleeping 9 hours or more per night also had increased odds ratios for DM and IGT. These associations persisted when subjects with insomnia symptoms were excluded.

Conclusions: A sleep duration of 6 hours or less or 9 hours or more is associated with increased prevalence of DM and IGT. Because this effect was present in subjects without insomnia, voluntary sleep restriction may contribute to the large public health burden of DM.

Arch Intern Med. 2005;165:863-868
OR of diabetes in <5h sleep vs 7-8h was 2.51 (1.57-4.02)
Shift work

Sleep disturbance

?

Insulin resistance
Type 2 diabetes
Shift work

Sleep disturbance

Altered circadian rhythms

Insulin resistance
Type 2 diabetes
Pancreatic beta cell
Melatonin and Insulin

- **Animal studies**
  - Pinealectomy results in hyperglycaemia and hyperinsulinaemia
  - Melatonin administration decreases insulin levels
Variants in *MTNR1B* influence fasting glucose levels

Pancreatic beta cell
Figure 2  Association of rs10830963 with type 2 diabetes (T2D) in 13 case-control studies.
Melatonin Secretion and the Incidence of Type 2 Diabetes

Ciaran J. McMullan, MD
Eva S. Schernhammer, MD, DrPH
Eric B. Rimm, ScD
Frank B. Hu, MD, PhD
John P. Forman, MD, MSc

Importance Loss-of-function mutations in the melatonin receptor are associated with insulin resistance and type 2 diabetes. Additionally, in a cross-sectional analysis of persons without diabetes, lower nocturnal melatonin secretion was associated with increased insulin resistance.

Objective To study the association between melatonin secretion and the risk of developing type 2 diabetes.

Design, Setting, and Participants Case-control study nested within the Nurses' Health Study cohort. Among participants without diabetes who provided urine and blood samples at baseline in 2000, we identified 370 women who developed type 2 diabetes from 2000-2012 and matched 370 controls using risk-set sampling.

Main Outcome Measures Associations between melatonin secretion at baseline and incidence of type 2 diabetes were evaluated with multivariable conditional logistic regression controlling for demographic characteristics, lifestyle habits, measures of sleep quality, and biomarkers of inflammation and endothelial dysfunction.

Results The median urinary ratios of 6-sulfatoxymelatonin to creatinine were 28.2 ng/mg (5%-95% range, 5.5-84.2 ng/mg) among cases and 36.3 ng/mg (5%-95% range, 6.9-110.8 ng/mg) among controls. Women with lower ratios of 6-sulfatoxymelatonin to creatinine had increased risk of diabetes (multivariable odds ratio, 1.48 [95% CI, 1.11-1.98] per unit decrease in the estimated log ratio of 6-sulfatoxymelatonin to creatinine). Compared with women in the highest ratio category of 6-sulfatoxymelatonin to creatinine, those in the lowest category had a multivariable odds ratio of 2.17 (95% CI, 1.18-3.98) of developing type 2 diabetes. Women in the highest category of melatonin secretion had an estimated diabetes incidence rate of 4.27 cases/1000 person-years compared with 9.27 cases/1000 person-years in the lowest category.

Conclusions and Relevance Lower melatonin secretion was independently associated with a higher risk of developing type 2 diabetes. Further research is warranted to assess if melatonin secretion is a modifiable risk factor for diabetes within the general population.

JAMA. 2013;309(13):1388-1396
Lowest quartile of urinary melatonin

Multivariate OR of developing T2 DM

2.17 (95% CI 1.18-3.98)
Shift work

Sleep disturbance

Altered circadian rhythms

Insulin resistance
Type 2 diabetes
12 healthy young males
Studied after 2 days of sleep restriction and then after 2 days of sleep extension
Controlled caloric intake and physical activity
Effect of shift work on diabetes?
Control of diabetes mellitus in shift workers

C J M Poole, A D Wright, M Nattrass

Table 1  Diabetic control in subjects on insulin working shifts (n = 16) or days only (n = 8), and in subjects taking oral hypoglycaemic drugs (n = 9)

<table>
<thead>
<tr>
<th></th>
<th>Blood glucose (mmol/l) Mean (SD)</th>
<th>Serum fructosamine (μmol/l) Mean (SD)</th>
<th>HbA1c (%) Mean (SD)</th>
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</thead>
<tbody>
<tr>
<td>Shifts on insulin</td>
<td>9·9 (4·2)</td>
<td>388 (70)</td>
<td>10·1 (1·9)</td>
</tr>
<tr>
<td>Days only on insulin</td>
<td>11·6 (3·7)</td>
<td>422 (66)</td>
<td>10·5 (1·8)</td>
</tr>
<tr>
<td>Oral hypoglycaemic drugs</td>
<td>10·5 (6·3)</td>
<td>365 (85)</td>
<td>10·0 (2·3)</td>
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</table>

None of the differences between groups was statistically significant.
Short Sleep Duration Measured by Wrist Actimetry Is Associated With Deteriorated Glycemic Control in Type 1 Diabetes

Figure 1—Distribution of HbA1c levels in patients with shorter (<6.5 h) vs. longer (>6.5 h) sleep duration. Comparisons between short vs. normal sleepers were determined using one-way ANOVA and were statistically significant (P = 0.001).
Control of type 1 diabetes mellitus and shift work

J. Young¹, E. Waclawski², J. A. Young³ and J. Spencer¹

¹OHSAS, Dundee, UK, ²NHS Greater Glasgow and Clyde, UK, ³NHS Tayside, UK.

Figure 1. HbA1c of non-shift (n = 164) and shift workers (n = 67) showing that shift workers have a higher HbA1c result (P < 0.05, t-test).
Shift work and diabetes?

1. Shift work is associated with adverse metabolic effects which may have a negative effect on managing diabetes
Shift work and diabetes?

1. Shift work is associated with adverse metabolic effects which may have a negative effect on managing diabetes
2. Shift work may not suit several treatment regimens for diabetes
Oral hypoglycaemic therapy
Oral hypoglycaemic therapy

Principally a problem in agents that can cause hypoglycaemia

- Metformin
- Sulphonylureas
- Pioglitazone
- DPP4 inhibitors (gliptins)
- SGLT2 inhibitors (gliflozins)
Oral hypoglycaemic therapy

1. Metformin – unlikely to cause hypoglycaemia but timing usually altered to reflect food intake
2. Sulphonylurea timing should match food intake
3. Other agents timing less important
Other injectables

GLP-1 agonists (exenatide, liraglutide, lixisenatide) are unlikely to cause hypoglycaemia and therefore timing not as important
Insulin
Insulin effect vs. Time (hours)

- **Rapid (Aspart, Glulisine, Lispro)**
- **Short (Regular)**
- **Intermediate (NPH)**
- **Long (Detemir, Glargine)**
“Advanced” insulin regimens

- Basal bolus insulin
- Insulin pump
Basal bolus insulin - basics

1. Once daily basal insulin (if dose correct) should remain unchanged whatever shift is being worked.
2. Bolus insulin should be administered with meals whenever they are taken.
Basal bolus - further adjustments
Basal bolus - further adjustments

1. Those on twice-daily basal insulin and insulin pumps will need to adjust their “day” and “night” background insulin depending on whether working or sleeping.

2. Bolus insulin to carbohydrate ratio will need assessed for overnight meals.
“Simpler” insulin regimens
“Simpler” insulin regimens

1. Basal Lantus or Levemir once daily
   ▫ No particular adjustments should be required
2. Basal insulatard or Humulin I once daily
   ▫ May be less suitable for shift work
“Simpler” insulin regimens

1. Basal Lantus or Levemir once daily
   - No particular adjustments should be required
2. Basal insulatard or Humulin I once daily
   - May be less suitable for shift work
3. Premixed insulin regimens (e.g. Novomix 30, Humalog Mix 25)
   - Unsuitable for shift work
Principles of diabetes care in shift work

1. Self-monitoring
   - Understand blood glucose patterns to allow treatment adjustments to be sensibly advised
Principles of diabetes care in shift work

2. Meal planning
   - Evenly spaced meals (4-5 hrs apart)
   - Consistent types and amounts of food
   - Understand when medication works and its duration of action when planning food
   - Readily available hypo treatment
Principles of diabetes care in shift work

3. Exercise
   - Be aware of the potential for exercise induced hypoglycaemia, especially overnight
Case 1

- Richard is a 47 yr old factory operator
- Type 2 diabetes for 6 yrs
- HbA1c 55 mmol/mol (7.2%)
- Metformin 1g bd
- Gliclazide 80mg bd
# Case 1

<table>
<thead>
<tr>
<th></th>
<th>Mon</th>
<th>Tues</th>
<th>Wed</th>
<th>Thurs</th>
<th>Fri</th>
<th>Sat</th>
<th>Sun</th>
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<tbody>
<tr>
<td>Wk 1</td>
<td>Early</td>
<td>Early</td>
<td>Early</td>
<td>Early</td>
<td>Early</td>
<td>Off</td>
<td>Off</td>
</tr>
<tr>
<td>Wk 2</td>
<td>Late</td>
<td>Late</td>
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<td>Off</td>
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<table>
<thead>
<tr>
<th>Early</th>
<th>Late</th>
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<tr>
<td>0600-1500h</td>
<td>1400h-2300h</td>
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</table>
Case 1

1. Anticipated meal times on both shifts
   ▫ “early” breakfast in work at 0800h
   lunch in work at 1200h
   dinner at home at 1700h

   ▫ “late” breakfast at home at 1000h
   lunch at work at 1600h
   dinner at work at 1900h
Case 1

1. Anticipated meal times on both shifts
   - “early” breakfast in work at 0800h
     lunch in work at 1200h
     dinner at home at 1700h
   - “late” breakfast at home at 1000h
     lunch at work at 1600h
     dinner at work at 1900h
Case 2

- Dawn is a 31yr midwife
- Type 1 diabetes for 16yrs
- HbA1c 50 mmol/mol (6.7%)
- DAFNE
  - Novorapid
    - Breakfast: 2 units per 10g CHO
    - Lunch: 1 unit per 10g CHO
    - Dinner: 1.5 units per 10g CHO
  - Lantus: 28 units at 2200h
- About to start Sunday & Monday night shifts
Case 2

1. Keep basal Lantus time and dose unchanged
2. Aim for regular meals and snacks throughout night shift
3. Cover these snacks with novorapid (initially on a 1 unit:10g CHO ratio)
4. Check sugars regularly to detect patterns of sugar levels
Metformin affects the circadian clock and metabolic rhythms in a tissue-specific manner

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Regulation of circadian behaviour and metabolism by synthetic REV–ERB agonists

Laura A. Solt1*, Yongjun Wang1*, Subhashis Banerjee1, Travis Hughes1, Douglas J. Kojetin1, Thomas Lundasen1, Youseung Shin2, Jin Liu1, Michael D. Cameron2, Romain Noel2, Seung-Hee Yoo3, Joseph S. Takahashi3, Andrew A. Butler4, Theodore M. Kamenecka2 & Thomas P. Burris1,5
Circadian gene expression

Per/Cry

Clock
Bmal1

PGC-1α

Rev-erba

RORα

PGC-1α

PGC-1α

Nuclear receptors/transcription factors

Energy metabolism
Activation of REV-ERB by SR9011 *in vivo* results in an increase in energy expenditure and weight loss.
Melatonin administration over 1 year to 1\textsuperscript{st} degree relatives of T2 diabetic patients assessing cardiometabolic risk