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Appendix 3

This appendix was part of the submitted manuscript and has been peer reviewed.
It is posted as supplied by the authors.

Appendix to: Twigg SM, Wong J. The imperative to prevent diabetes complications: a broadening spectrum and an increasing burden despite improved outcomes. *Med J Aust* 2015; 202: 300-304. doi: 10.5694/mja14.01234.

Appendix 3. *Potential Future Initiatives to Aid Complications Management*

Prospective potential directions in complications research and care	**Potential related clinical use in diabetes complications**
Genotyping of diabetes complications risk and developing personalised '*complications risk algorithms*' for each main complication	Improved stratification of complications prevention and screening to high risk patients and reassuring those at low risk
Methods for *increased sensitivity* of detection of organ complications by subclinical screening - for renal function (cystatin C); unstable coronary plaque (intravascular ultrasound imaging); incipient foot ulceration (eg localised cutaneous heat) and retinopathy screening (ultra wide field digital retinal camera imaging)	Targeting of complications prevention and progression to patients who are developing early significant phenotypic changes of complications and are thus at increased risk of progression and require specific intervention
Increased *breadth* of routine complications screening– diabetic cardiomyopathy; NAFLD in diabetes; sleep apnoea; gastroparesis and cardiac autonomic neuropathy; cognitive decline, developing dementia; certain cancers (eg colo-rectal, breast, liver)	Detecting diabetes-related comorbidities in a timely manner and managing them
New methods to monitor and treat *reversible risk factors* such as glucose (smart insulins; closed loop technology), lipids (combined and improved agents), blood pressure (regular ambulatory blood pressure), and improved nutrient, exercise and body weight recommendations.	Targeting reversible metabolic and haemodynamic risk factors for diabetes complications in a more effective manner; defining who will best benefit from types of bariatric surgery
New treatments for *complications mediators* (advanced glycation cross-link breakers, growth factor targeting; anti-inflammatory and fibrosis therapies)	In those with specific clinical diabetes complications the complication can be stabilised, and possibly reversed.
New autografted *organ replacement* incl. stem cell and 3D printing technology	All affected organ sites – eye, heart, legs, kidney, liver, pancreas