MASSACHUSETTS

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Medical Policy

Multianalyte Assays with Algorithmic Analyses for Predicting Risk of Type 2 Diabetes

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Policy Number: 654

BCBSA Reference Number: 2.04.90A
NCD/LCD: N/A

Related Policies

None

Policy

Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO Blue[SM] and Medicare PPO Blue[SM] Members

The use of multianalyte panels with algorithmic analysis (MAAA) for the prediction of type 2 diabetes is **INVESTIGATIONAL**.

Prior Authorization Information

Inpatient

- For services described in this policy, precertification/preauthorization **IS REQUIRED** for all products if the procedure is performed **inpatient**.

Outpatient

- For services described in this policy, see below for products where prior authorization **might be required** if the procedure is performed **outpatient**.

	Outpatient
Commercial Managed Care (HMO and POS)	This is **not** a covered service.
Commercial PPO and Indemnity	This is **not** a covered service.
Medicare HMO Blue[SM]	This is **not** a covered service.
Medicare PPO Blue[SM]	This is **not** a covered service.

CPT Codes / HCPCS Codes / ICD Codes

Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

CPT Codes

CPT codes:	Code Description
81506	Endocrinology (type 2 diabetes), biochemical assays of seven analytes (glucose, HbA1c, insulin, hs-CRP, adiponectin, ferritin, interleukin 2-receptor alpha), utilizing serum or plasma, algorithm reporting a risk score

Description

The Pre-Dx® Diabetes Risk Score (DRS) is a multianalyte assay with algorithmic analysis (MAAA) that is intended to predict the 5-year risk of type 2 diabetes. It is composed of 7 serum biomarkers that are combined via a proprietary algorithm. The proposed use is to identify patients at greater risk of developing type 2 diabetes, and to potentially target preventive interventions at patients with the highest risk.

Background

Type 2 diabetes mellitus is a highly prevalent disorder that is associated with an extremely high degree of morbidity and mortality. The true prevalence of type 2 diabetes in the U.S. is uncertain due to a lack of population screening, but an estimated prevalence of 8.2% was reported in 2006. (1) The incidence has been increasing rapidly over the last several decades, and current trends indicate that this increase will continue. (2) Projections have estimated that the prevalence in the U.S. will reach 11.5% in 2011, 13.5% in 2021, and 14.5% in 2031. (3)

Therefore, there is an urgent public health need to counter this trend. The potential to improve outcomes and reduce costs by preventing the onset of diabetes is vast. In order to accomplish this, accurate risk prediction methods may be helpful to identify populations with the highest risk of diabetes. Identification of patients at high risk could then be followed by preventive interventions targeted at high-risk individuals.

Predicting risk of type 2 diabetes. There are a variety of known factors that predict risk of type 2 diabetes. The most direct are measures of glucose metabolism, such as fasting glucose, oral glucose tolerance testing (OGTT), and hemoglobin A1C (HgA1C). For patients with impaired fasting glucose (IFG) or impaired glucose tolerance (IGT), there is a high rate of progression to diabetes. Approximately 10% of these patients will progress to diabetes each year, and by 10 years more than 50% will have progressed to diabetes. (4)

Other risk factors for diabetes include family history, ethnicity, lifestyle factors, dietary patterns, and numerous different laboratory parameters. A history of diabetes in the immediate family has long been recognized as one of the strongest predictors of diabetes. Regarding ethnicity, the risk of diabetes is increased 1.34 times for blacks, 1.86 times for Hispanics, and 2.26 times for Asians. (5) A sedentary lifestyle, cigarette smoking, and dietary patterns that include sweetened foods and beverages have all been positively associated with the development of diabetes. In addition, there are numerous non-glucose laboratory parameters that are associated with the risk of diabetes. These include inflammatory markers, lipid markers, measures of endothelial dysfunction, sex hormones, and many others. (6, 7)

Formal risk prediction instruments have combined clinical, laboratory, and genetic information to improve and refine upon the predictive ability of single factors. Many different formal risk prediction models have been developed. These models vary in the number and type of factors examined, and in the intended use of the instrument. For example, some prediction instruments consider the full range of clinical, biochemical, and genetic factors in order to derive the most accurate predictive model. (8) Others, such as the Indian Risk Score, use easily available clinical information without any laboratory markers in order to facilitate implementation as a widespread screening tool in areas of low resources. (9)

In general, the available models have been shown to have good predictive ability, but most of them have not been externally validated. There is some evidence that directly compares the predictive accuracy of different measures, but there is insufficient comparative research to determine the optimal model. There is evidence that different models have different accuracy depending on the population tested. Also, relatively simple models have performed similarly to more complex models, and genetic information seems to add little over readily available clinical and metabolic parameters. (10)

Interventions to prevent type 2 diabetes. A number of intervention trials have established that both lifestyle interventions and medications are effective in preventing the onset of type 2 diabetes in high-risk individuals. These trials have selected patients at high risk for diabetes, but have used single or several clinical factors, such as impaired glucose metabolism as selection factors, rather than formal risk prediction instruments. The largest reduction in diabetes incidence has been found for intensive lifestyle interventions that combine exercise and diet. There is a lesser effect for interventions with a single component and for interventions with medications.

A Cochrane review on the efficacy of lifestyle interventions to prevent type 2 diabetes was published in 2008. (11) This review included eight randomized trials that compared exercise and dietary interventions to standard therapy in patients at high risk for diabetes. There was a 37% reduction in the incidence of diabetes for the intervention cohort when a combined diet/exercise intervention was used, but there were not significant effects noted for an exercise-only or a diet-only intervention.

Another systematic review and meta-analysis evaluated the efficacy of medications for preventing progression to type 2 diabetes. (12) This review included 10 studies of oral hypoglycemic agents and 15 studies of injectable agents. Oral hypoglycemic agents and orlistat were found to be effective in reducing progression to diabetes compared to usual care. In the largest trials with follow-up of greater than 2 years, metformin (relative risk [RR]: 0.69, 95% confidence interval [CI]: 0.57-0.83), acarbose (0.75, 0.63-0.90), troglitazone (0.45, 0.25-0.83), and orlistat (hazard ratio [HR]: 0.63, 95% CI: 0.46-0.86) were efficacious in decreasing diabetes incidence compared with placebo. Evidence for other medication such as statins, fibrates, antihypertensive agents, and estrogen was inconclusive.

The largest randomized trial of preventive interventions was the Diabetes Prevention Program trial. (13) This trial enrolled 3,234 obese patients with a high risk of diabetes as defined by body mass index (BMI) level, fasting glucose, and 2-hour post-prandial glucose levels. Participants were randomized to one of three groups, an intensive lifestyle intervention, a medication intervention consisting of metformin (850 mg twice per day), or a placebo control with information provided on diet and exercise. After a mean follow-up of 3 years, the incidence of diabetes was significantly reduced by 58% in the intensive lifestyle intervention group, and by 31% in the metformin group. A follow-up observational study concluded that the bulk of the benefit persisted for at least 10 years following completion of the trial. (14)

Pre-Dx® Diabetes Risk Score

The Pre-Dx® Diabetes Risk Score™ (Tethys Bioscience®, Inc., Emeryville, CA) is a commercially available multianalyte assay with algorithmic analysis (MAAA) that is intended to determine the 5-year risk of developing type 2 diabetes. The risk score is based on 7 biomarkers that are obtained by a peripheral blood draw:

- HgA1C
- Glucose
- Insulin
- C-reactive protein
- Ferritin
- Adiponectin
- Interleukin-2 receptor alpha

The results of these biomarkers are combined with age and gender to produce a quantitative risk score that varies from 0 to 10. Results are reported as the absolute 5-year risk of developing type 2 diabetes and the relative risk compared to age and gender matched controls.

Summary

The Pre-Dx® diabetes risk score is a multianalyte assay with algorithmic analyses (MAAA) that uses 7 biomarkers, including glucose and HgA1C, to predict progression to diabetes. There is limited published evidence on the validity and applicability of this risk score. Two patient cohorts reported areas under the curve (AUCs) for predicting progression to diabetes that ranged from 0.78-0.84. This suggests good overall predictive ability, but is limited by the lack of validation by independent research groups and testing in a wider variety of patient populations. The evidence is insufficient to determine the comparative accuracy of the Pre-Dx® diabetes risk score with other formal prediction models for diabetes.

There is a lack of evidence on the clinical utility of the Pre-Dx® score. No published studies were identified that used the risk score to select patients for preventive interventions. As a result, it is not known how this instrument will perform in targeting preventive interventions to patients who will benefit the most, nor is it known how this risk score compares to other methods for selecting high-risk patients. Therefore, use of the Pre-Dx® diabetes risk score is considered investigational.

Policy History

Date	Action
4/2020	Policy updated with literature review through March 20, 2020, no references added. Policy statements unchanged.
11/2019	ICD-9 reference removed.
3/2015	New references added from BCBSA National medical policy.
5/2014	New references from BCBSA National medical policy.
8/2013	BCBSA National medical policy review. New policy describing investigational indications. Effective 8/1/2013.

Information Pertaining to All Blue Cross Blue Shield Medical Policies

Click on any of the following terms to access the relevant information:
Medical Policy Terms of Use
Managed Care Guidelines
Indemnity/PPO Guidelines
Clinical Exception Process
Medical Technology Assessment Guidelines

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