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The Impact of Supplementing Traditional Risk Information with Polygenic Risk Score Concerning Type 2 Diabetes and Coronary Heart Disease on Health Behavior: A Randomized Controlled Trial

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Supplementary File 2

Intervention Materials (Example)

Figure 1. Internet portal Feedback Example Concerning Type 2 Diabetes Results Part 1

A Type 2 diabetes

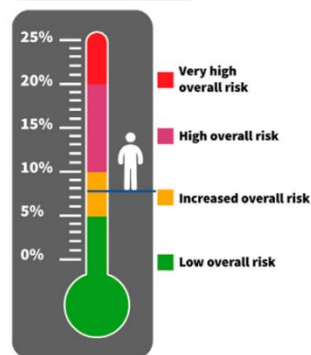
Overall risk of type 2 diabetes

We have calculated your overall risk of developing type 2 diabetes. This assessment has taken into account your polygenic risk score (PRS) and traditional risk factors associated with type 2 diabetes (gender, BMI, cholesterol, lipid-lowering medication, antihypertensive medication, systolic blood pressure, smoking and family history of the disease).

The lifestyle values have been obtained from the FinHealth 2017 study. If a value has been missing, the average value for the population of the same age and gender has been used.

For people under 24 years of age, we have used age 24 for calculating the risk estimates. Similarly for people over 75 years of age, age 75 has been used for risk estimates.

Show the lifestyle values used



Taking into account the traditional risk factors related to type 2 diabetes as well as hereditary predisposition, your risk of developing type 2 diabetes in the next 10 years is 7.8%.

B

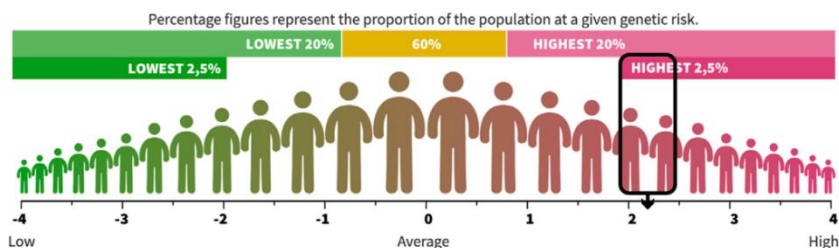
Genetic predisposition for type 2 diabetes

The hereditary, i.e. genetic, risk only describes the effect your genome has on developing type 2 diabetes.

This study involved testing nearly 7 million sections of the human genome, or gene variants, which scientific research has found to be connected to type 2 diabetes. Your personal polygenic risk score was formed out of these genome sections.

Your genetic risk is examined by comparing it to the population's average genetic risk. The average genetic risk value for the population is 0, i.e. the risk will neither grow nor decline based on the influence of the genome. For 60% of the population, the genetic risk score is between -0.86 and 0.86. The lower your value (-4-0), the fewer gene variants in your genome expose you to type 2 diabetes. The higher your value (0-4) the more gene variants in your genome expose you to type 2 diabetes.

Your polygenic risk score is 2.21 (highest 2,5% in population), which means that your **genetic risk** of developing type 2 diabetes is significantly higher than most of the population.

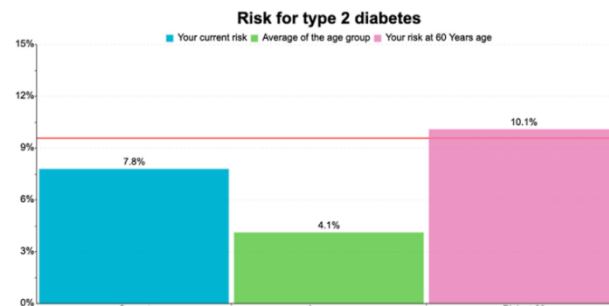


Note. (A) The absolute (overall) risk was presented as a thermometer. The risk limits for T2D were 0-5% (low), 5-10% (elevated), 10-20% (high), >20% (very high). (B) PRS was presented as a single value in relation to the whole population on a normal distribution curve. Image is taken from Marjonen et al., 2021.

Figure 2. Internet portal Feedback Example Concerning Type 2 Diabetes Results Part 2

A The risk of developing type 2 diabetes within the next 10 years

In the below descriptor, the left column describes your present risk of developing type 2 diabetes with your current lifestyle values (gender, BMI, cholesterol, lipid-lowering medication, antihypertensive medication, systolic blood pressure, smoking and family history of the disease). Your risk of developing type 2 diabetes within the next 10 years is 7.8%.



The column in the centre presents the average disease risk of population of the same age and on the right your risk of developing the disease at the age of 60 without changes in your lifestyle factors.

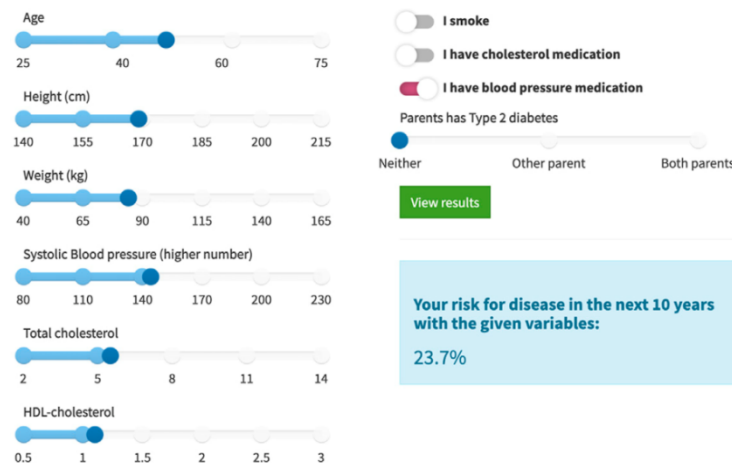
The red horizontal line represents a 10% risk of illness over the next 10 years. The risk of over 10% is high and well above the average risk of the population.

Instructions for physicians

B

Try the risk calculator

You can influence your blood pressure, cholesterol values and other disease risk factors with lifestyle. Changing your values in the calculator allows you to see how a change in your lifestyle could reduce your risk of developing the disease within the next 10 years.



Note. (A) The three columns from left to right present: participant's absolute risk at current age, average absolute risk in similar age population, and participant's estimated 10-years risk at the age of 60. Red line at 10% presents the "high" risk threshold. (B) Participants were able to change their lifestyle factors in a risk calculator which could be seen as changes in the above risk columns. Image is taken from Marjonen et al., 2021.

In addition to the information presented in Figures 1 and 2, participants also received a doctor's note providing a more detailed explanation of their results. Below, example reports on T2D are presented for different age and risk groups. **All text and images are taken from Marjonen et al., 2021.**

This model for under-50-year-olds

Assessment of your risk of developing type 2 diabetes

You may present this information sheet to your physician

Dear NN,

Type 2 diabetes is caused by a metabolism dysfunction that decreases insulin production and reduces the effect of insulin. The disease gradually develops over several years, often without symptoms, and can be detected accidentally. As the disease progresses, the person's risk of developing a vascular disorder and other additional illnesses grows. Around 300,000 people are known to have type 2 diabetes in Finland. In addition to age, lifestyle and genetic factors influence the risk of developing the disease.

The information collected from you in the FinHealth study included your gender, BMI, cholesterol, lipid-lowering medication, antihypertensive medication, systolic blood pressure, smoking and family history of the disease, and used as the basis for calculating your risk of developing type 2 diabetes. We also used these values in this study. If one of these measurement results was not available for you, we used the average value of the population. We supplemented the risk assessment based on this information with a risk assessment based on genes. We examined nearly 7 million of your gene variants and used them to estimate your genetic risk of developing type 2 diabetes. The combined impact of the gene variants is described with the PRS value (polygenic risk score, or the combined impact of several different genetic factors). You can view your personal PRS, or polygenic risk score, in your personal results at the MyP5 website.

Different texts for 4 different risk groups:

For the group: risk >20%

Your MyP5 website includes our assessment of your likelihood for developing type 2 diabetes within the next ten years. The risk of type 2 diabetes grows as people age. As a result, we have also estimated your risk of developing diabetes based on your lifestyle and genes within the next ten years if you were currently 50 years old and had not yet been diagnosed with diabetes at that age.

Based on our estimate, your risk of developing type 2 diabetes at the age of 50–60 is over 20%, which is very high and clearly above the average risk level in the population. In other words: out of one hundred people with a similar lifestyle and genes as you, more than 20 will probably develop diabetes at the age of 50–60. The risk assessment presumes that your lifestyle remains as it is currently. This assessment has not taken into account very rare gene variants affecting inherited forms of diabetes.

We recommend that you show this message to a physician or public health nurse at a health centre or in occupational health care, for instance. A risk assessment this high indicates that you are at a risk of developing the disease at a much younger age than average. As a result, it would be highly important for the health care services to evaluate on a case-by-case basis what sort of guidance and support you need in implementing lifestyle changes and when there will be need to monitor your blood values to detect the onset of diabetes.

Your genes stay the same throughout your entire life. However, a healthy lifestyle can highly significantly reduce your risk of developing a disease or postpone the onset of a disease by several years. It is particularly important to engage in physical activity, eat healthily and aim at maintaining a normal weight. Even a minor weight loss will reduce the risk. It is also important not to smoke. Good instructions are available at the Finnish Diabetes Association website at www.diabetes.fi.

For the group: risk >10% <20%

Your MyP5 website includes our assessment of your likelihood for developing type 2 diabetes within the next ten years. The risk of type 2 diabetes grows as people age. As a result, we have also estimated your risk of developing diabetes based on your lifestyle and genes within the next ten years if you were currently 50 years old and had not yet been diagnosed with diabetes at that age.

Based on our estimate, your risk of developing type 2 diabetes at the age of 50–60 is over 10–20%, which is high and above the average risk level in the population. In other words: out of one hundred people with a similar lifestyle and genes as you, around 10–20 will probably develop diabetes at the age of 50–60. The risk assessment presumes that your lifestyle remains as it is currently. This assessment has not taken into account very rare gene variants affecting inherited forms of diabetes.

We recommend that you show this message to a physician or public health nurse at a health centre or in occupational health care, for instance. A risk assessment this high indicates that you may be at a risk of developing the risk before the age of 50–60. As a result, it would be good for the health care services to evaluate on a case-by-case basis what sort of guidance and support you need in implementing lifestyle changes and when there will be need to monitor your blood values to detect the onset of diabetes.

Your genes stay the same throughout your entire life. However, a healthy lifestyle can highly significantly reduce your risk of developing a disease or postpone the onset of a disease by several years. It is particularly important to engage in physical activity, eat healthily and aim at maintaining a normal weight. Even a minor weight loss will reduce the risk. It is also important not to smoke. Good instructions are available at the Finnish Diabetes Association website at www.diabetes.fi.

For the group: risk >5% <10%

Your MyP5 website includes our assessment of your likelihood for developing type 2 diabetes within the next ten years. The risk of type 2 diabetes grows as people age. As a result, we have also estimated your risk of developing diabetes based on your lifestyle and genes within the next ten years if you were currently 50 years old and had not yet been diagnosed with diabetes at that age.

Based on our estimate, your risk of developing type 2 diabetes at the age of 50–60 is 5–10%. This is a slightly elevated result and above the average population risk. In other words: out of

one hundred people with a similar lifestyle and genes as you, 5–10 will probably develop diabetes at the age of 50–60. The risk assessment presumes that your lifestyle remains as it is currently. This assessment has not taken into account very rare gene variants affecting inherited forms of diabetes.

Your genes stay the same throughout your entire life. However, a healthy lifestyle can highly significantly reduce your risk of developing a disease or postpone the onset of a disease by several years. It is particularly important to engage in physical activity, eat healthily and aim at maintaining a normal weight. Even a minor weight loss will reduce the risk. It is also important not to smoke.

You can show this message to a physician or public health nurse at a health centre or in occupational health care, for instance, to receive guidance and support for implementing lifestyle changes. Good instructions are available at the Finnish Diabetes Association website at www.diabetes.fi.

For the group: risk <5%

Your MyP5 website includes our assessment of your likelihood for developing type 2 diabetes within the next ten years. The risk of type 2 diabetes grows as people age. As a result, we have also estimated your risk of developing diabetes based on your lifestyle and genes within the next ten years if you were currently 50 years old and had not yet been diagnosed with diabetes at that age.

Based on our estimate, your risk of developing type 2 diabetes at the age of 50–60 is less than 5%. This result is equal to the average population rates. In other words: out of one hundred people with a similar lifestyle and genes as you, less than 5 will probably develop diabetes at the age of 50–60. The risk assessment presumes that your lifestyle remains as it is currently. This assessment has not taken into account very rare gene variants affecting inherited forms of diabetes.

Your genes stay the same throughout your entire life. However, a healthy lifestyle can highly significantly reduce your risk of developing a disease or postpone the onset of a disease by several years. It is particularly important to engage in physical activity, eat healthily and aim at maintaining a normal weight. It is also important not to smoke. Good instructions are available at the Finnish Diabetes Association website at www.diabetes.fi.

This model for 50-75-year-olds

Assessment of your risk of developing type 2 diabetes

You may present this information sheet to your physician.

Dear NN,

Type 2 diabetes is caused by a metabolism dysfunction that decreases insulin production and reduces the effect of insulin. The disease gradually develops over several years, often without symptoms, and can be detected accidentally. As the disease progresses, the person's risk of developing a vascular disorder and other additional illnesses grows. Around 300,000 people are known to have type 2 diabetes in Finland. In addition to age, lifestyle and genetic factors influence the risk of developing the disease.

The information collected from you in the FinHealth study included your gender, BMI, cholesterol, lipid-lowering medication, antihypertensive medication, systolic blood pressure, smoking and family history of the disease, and used as the basis for calculating your risk of developing type 2 diabetes. We also used these values in this study. If one of these measurement results was not available for you, we used the average value of the population. We supplemented the risk assessment based on this information with a risk assessment based on genes. We examined nearly 7 million of your gene variants and used them to estimate your genetic risk of developing type 2 diabetes. The combined impact of the gene variants is described with the PRS value (polygenic risk score, or the combined impact of several different genetic factors). You can view your personal PRS, or polygenic risk score, in your personal results at the MyP5 website.

Different texts for 4 different risk groups:

For the group: risk >20%

The risk of type 2 diabetes grows as people age. Below, we evaluate your risk of developing type 2 diabetes within the next ten years if you have not yet been diagnosed with diabetes. **Based on our estimate, your risk of developing type 2 diabetes within the next ten years is over 20%, which is very high and clearly above the average risk level in the population.** In other words: out of one hundred people with a similar lifestyle and genes as you, more than 20 will probably develop type 2 diabetes within the next ten years. The risk assessment presumes that your lifestyle remains

as it is currently. This assessment has not taken into account very rare gene variants affecting inherited forms of diabetes.

We recommend that you show this message to a physician or public health nurse at a health centre or in occupational health care, for instance. We think it would be highly important for the health care services to evaluate on a case-by-case basis what sort of guidance and support you need in implementing lifestyle changes and when there will be need to monitor your blood values to detect the onset of diabetes.

Your genes stay the same throughout your entire life. However, a healthy lifestyle can highly significantly reduce your risk of developing a disease or postpone the onset of a disease by several years. It is particularly important to engage in physical activity, eat healthily and aim at maintaining a normal weight. Even a minor weight loss will reduce the risk. It is also important not to smoke. Good instructions are available at the Finnish Diabetes Association website at www.diabetes.fi.

For the group: risk >10% <20%

The risk of type 2 diabetes grows as people age. Below, we evaluate your risk of developing type 2 diabetes within the next ten years if you have not yet been diagnosed with diabetes. **Based on our estimate, your risk of developing type 2 diabetes within the next ten years is 10–20%, which is high compared to the average risk level in the population.** In other words: out of one hundred people with a similar lifestyle and genes as you, 10–20 will probably develop type 2 diabetes within the next ten years. The risk assessment presumes that your lifestyle remains as it is currently. This assessment has not taken into account very rare gene variants affecting inherited forms of diabetes.

We recommend that you show this message to a physician or public health nurse at a health centre or in occupational health care, for instance. We think it would be good for the health care services to evaluate on a case-by-case basis what sort of guidance and support you need in implementing lifestyle changes and when there will be need to monitor your blood values to detect the onset of diabetes.

Your genes stay the same throughout your entire life. However, a healthy lifestyle can highly significantly reduce your risk of developing a disease or postpone the onset of a disease by several years. It is particularly important to engage in physical activity, eat healthily and aim at maintaining a normal weight. Even a minor weight loss will reduce the risk. It is also important not to smoke. Good instructions are available at the Finnish Diabetes Association website at www.diabetes.fi.

For the group: risk >5% <10%

The risk of type 2 diabetes grows as people age. Below, we evaluate your risk of developing type 2 diabetes within the next ten years if you have not yet been diagnosed with diabetes. **Based on our estimate, your risk of developing type 2 diabetes within the next ten years is 5–10 %. While this is not particularly high compared to the average population risk, it is nevertheless worth considering.** In other words: out of one hundred people with a similar lifestyle and genes as you, 5–10 will probably develop diabetes within the next ten years. The risk assessment presumes that your lifestyle remains as it is currently. This assessment has not taken into account very rare gene variants affecting inherited forms of diabetes.

Your genes stay the same throughout your entire life. However, a healthy lifestyle can highly significantly reduce your risk of developing a disease or postpone the onset of a disease by several years. It is particularly important to engage in physical activity, eat healthily and aim at maintaining a normal weight. Even a minor weight loss will reduce the risk. It is also important not to smoke.

You can show this message to a physician or public health nurse at a health centre or in occupational health care, for instance, to receive guidance and support for implementing lifestyle changes. Good instructions are available at the Finnish Diabetes Association website at www.diabetes.fi.

For the group: risk <5%

The risk of type 2 diabetes grows as people age. Below, we evaluate your risk of developing type 2 diabetes within the next ten years if you have not yet been diagnosed with diabetes. **Based on our estimate, your risk of developing type 2 diabetes within the next ten years is less than 5%. In your age group, this is a fairly low risk compared to the average population risk.** In other words: out of one hundred people with a similar lifestyle and genes as you, fewer than 5 will probably develop type 2 diabetes within the next ten years. The risk assessment presumes that your lifestyle remains as it is currently. This assessment has not taken into account very rare gene variants affecting inherited forms of diabetes.

Your genes stay the same throughout your entire life. However, **a healthy lifestyle can further reduce your risk of developing a disease or postpone the onset of a disease by several years.** It is particularly important to engage in physical activity, eat healthily and aim at maintaining a normal weight. Even a minor weight loss will reduce the risk. It is also important not to smoke. Good instructions are available at the Finnish Diabetes Association website at www.diabetes.fi.

This model for over-75-year-olds.

Assessment of your risk of developing type 2 diabetes

You may present this information sheet to your physician

Dear NN,

Type 2 diabetes is caused by a metabolism dysfunction that decreases insulin production and reduces the effect of insulin. The disease gradually develops over several years, often without symptoms, and can be detected accidentally. As the disease progresses, the person's risk of developing a vascular disorder and other additional illnesses grows. Around 300,000 people are known to have type 2 diabetes in Finland. In addition to age, lifestyle and genetic factors influence the risk of developing the disease.

The information collected from you in the FinHealth study included your gender, BMI, cholesterol, lipid-lowering medication, antihypertensive medication, systolic blood pressure, smoking and family history of the disease, and used as the basis for calculating your risk of developing type 2 diabetes. We also used these values in this study. If one of these measurement results was not available for you, we used the average value of the population. We supplemented the risk assessment based on this information with a risk assessment based on genes. We examined nearly 7 million of your gene variants and used them to estimate your genetic risk of developing type 2 diabetes. The combined impact of the gene variants is described with the PRS value (polygenic risk score, or the combined impact of several different genetic factors). You can view your personal PRS, or polygenic risk score, in your personal results at the MyP5 website.

Different texts for 4 different risk groups:

For the group: risk >20%

The risk of type 2 diabetes grows as people age. **According to our results, at the age of 75, your risk of developing diabetes within the next ten years was over 20%.** In other words: out of one hundred people aged 75 with a similar lifestyle and genes as you, more than 20 will probably develop diabetes within a few coming

years. The risk assessment presumes that the persons have not yet been diagnosed with diabetes and their lifestyle remains as it is currently. **This risk is high, and it can also be considered**

indicative at your current age even though it is not possible to calculate a clear risk assessment to research participants over 75 years of age based on our research data. This assessment has not taken into account very rare gene variants affecting inherited forms of diabetes.

We recommend that you show this message to a physician or public health nurse at a health centre, for instance. We think it would be highly important for the health care services to evaluate on a case-by-case basis what sort of guidance and support you need in implementing lifestyle changes and when there will be need to monitor your blood values to detect the onset of diabetes.

Your genes stay the same throughout your entire life. However, a healthy lifestyle can highly significantly reduce your risk of developing a disease or postpone the onset of a disease by several years. It is particularly important to engage in physical activity, eat healthily and aim at maintaining a normal weight. Even a minor weight loss will reduce the risk. It is also important not to smoke. Good instructions are available at the Finnish Diabetes Association website at www.diabetes.fi.

For the group: risk >10% <20%

The risk of type 2 diabetes grows as people age. **According to our results, at the age of 75, your risk of developing diabetes within the next ten years was over 10–20%.** In other words: out of one hundred people aged 75 with a similar lifestyle and genes as you, 10–20 will probably develop diabetes within a few coming years. The risk assessment presumes that the persons have not yet been diagnosed with diabetes and their lifestyle remains as it is currently. **This risk is fairly high, and it can also be**

considered indicative at your current age even though it is not possible to calculate a clear risk assessment to research participants over 75 years of age based on our research data. This assessment has not taken into account very rare gene variants affecting inherited forms of diabetes.

We recommend that you show this message to a physician or public health nurse at a health centre, for instance. We think it would be good for the health care services to evaluate on a case-by-case basis what sort of guidance and support you need in implementing lifestyle changes and when there will be need to monitor your blood values to detect the onset of diabetes.

Your genes stay the same throughout your entire life. However, a healthy lifestyle can highly significantly reduce your risk of developing a disease or postpone the onset of a disease by several years. It is particularly important to engage in physical activity, eat healthily and aim at maintaining a normal weight. Even a minor weight loss will reduce the risk. It is also important not to smoke. Good instructions are available at the Finnish Diabetes Association website at www.diabetes.fi.

For the group: risk >5% <10%

The risk of type 2 diabetes grows as people age. **According to our results, at the age of 75, your risk of developing diabetes within the next ten years was over 5-10 %.** In other words: out of one hundred people aged 75 with similar lifestyle and genes as you, 5-10 will probably develop diabetes within a few coming years. The risk assessment presumes that the persons have not yet been diagnosed with diabetes and their lifestyle remains as it is currently. **While this risk is not high compared to the average population risk, it is nevertheless worth considering. It can also be considered indicative at your current age even though it is not possible to calculate a clear**

risk assessment to research participants over 75 years of age based on our research data. This assessment has not taken into account very rare gene variants affecting inherited forms of diabetes.

Your genes stay the same throughout your entire life. However, a healthy lifestyle can highly significantly reduce your risk of developing a disease or postpone the onset of a disease by several years. It is particularly important to engage in physical activity, eat healthily and aim at maintaining a normal weight. Even a minor weight loss will reduce the risk. It is also important not to smoke.

You can show this message to a physician or public health nurse at a health centre, for instance, to receive guidance and support for implementing lifestyle changes. Good instructions are available at the Finnish Diabetes Association website at www.diabetes.fi.

For the group: risk <5%

The risk of type 2 diabetes grows as people age. **According to our results, at the age of 75, your risk of developing diabetes within the next ten years was less than 5%.** In other words: out of one hundred people aged 75 with a similar lifestyle and genes as you, less than 5 will probably develop diabetes within a few coming years. The risk assessment presumes that the persons do not yet have diabetes and their lifestyle remains as it is currently. **This risk is fairly low in the age group of 75-year-olds, and it can also be considered indicative at your current age even though it is not possible to calculate a clear risk assessment to research participants over 75 years of age based on our research data.** This assessment has not taken into account very rare gene variants affecting inherited forms of diabetes.

Your genes stay the same throughout your entire life. However, **a healthy lifestyle can further reduce your risk of developing a disease or postpone the onset of a disease by several years.** It is particularly important to engage in physical activity, eat healthily and aim at maintaining a normal weight. Even a minor weight loss will reduce the risk. It is also important not to smoke. Good instructions are available at the Finnish Diabetes Association website at www.diabetes.fi.

References

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