

## Pre-screening tools for diabetes and obesity-associated dyslipidaemia: comparing BMI, waist and waist hip ratio. The D.E.S.I.R. Study

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## Abstract

**Objective:** To compare the sensitivities of BMI, waist circumference and waist hip ratio (WHR) in identifying subjects who should be screened for diabetes and/or for obesity-associated dyslipidaemia.

5 **Design:** Cross-sectional study.

**Setting:** Central-western France.

**Participants:** More than 3000 men and women, aged 40 to 64 years, from the French study: Data from an Epidemiological Study on the Insulin Resistance syndrome (D.E.S.I.R.).

10 **Main outcome measures:** Sensitivity and specificity for screened diabetes (fasting plasma glucose  $\geq 7.0$  mmol/l) and screened dyslipidaemia (triglycerides  $\geq 2.3$  mmol/l and/or HDL-cholesterol  $< 0.9/1.1$  mmol/l (men/women)) according to BMI, waist circumference and WHR..

15 **Results:** Sensitivities increased as more corpulent subjects were screened, but they increased slowly after screening the top 30%: BMI  $\geq 27/26$  kg/m<sup>2</sup> (men/women) or waist  $\geq 96/83$  cm or WHR  $\geq 0.96/0.83$ . These values were chosen as thresholds. In men, BMI had a non-significantly higher sensitivity than waist or WHR for both diabetes and dyslipidaemia (77% vs 74% and 66%  $P < 0.3, 0.09$ ; 56% vs 54% and 49%  $P < 0.5, 0.16$ ). For women, waist had a slightly higher sensitivity than BMI or WHR (82% vs 77% and 77%  $P < 0.8, 0.7$ ) for diabetes; for dyslipidaemia, waist and WHR had similar sensitivities, higher than for BMI (65% and 67% vs 54%  $P < 0.16, 0.13$ ).

20 **Conclusions:** We propose that for screening in a French population 40 to 64 years of age, the more obese 30% of the population, identified either by BMI, waist or WHR be screened for diabetes and obesity-associated dyslipidaemia.

**Keywords:** diabetes, dyslipidaemia, screening, obesity, waist

**Abbreviations:** BMI, body mass index; WHR, waist hip ratio

## Introduction

The metabolic syndrome is accompanied by obesity and Bjorntorp (1988), Kissebah and Peiris (1989), Després *et al.* (2001) have provided us with a number of hypotheses as to the importance of central obesity in metabolic regulation. Metabolic parameters, glucose, insulin, lipids, are positively associated with an increase in central adiposity: even after adjusting for BMI, the waist hip ratio (WHR) is positively associated with these parameters, with an almost continuous relation, which is independent of sex (Bertrais *et al.*, 1999). These physiological and statistical relations are not questioned. However the utility of the waist circumference and/or the WHR, over the BMI, in the identification of subjects who could benefit from screening for diabetes and for obesity-associated lipid disorders (hypertriglyceridaemia and hypo-HDL-cholesterolaemia) merits study. The current American Diabetes Association recommendations for diabetes screening are “3-year intervals beginning at age 45 years, particularly in those with BMI  $\geq$  25 kg/m<sup>2</sup> ” (ADA, 2004). There appears to be no equivalent recommendations for screening for obesity-associated dyslipidaemia.

Several diabetes risk score tests have been developed, in both the United States and in Europe, however they are not always comparable as the criteria used for the diagnosis of diabetes differ (ADA, 2000; Baan *et al.*, 1999; Glumer *et al.*, 2004; Griffin *et al.*, 2000; Herman *et al.*, 1995; Ruige *et al.*, 1997; The Expert Committee, 1997; WHO, 1985; WHO, 1999;) The most recent risk score comes from Denmark (Glumer *et al.*, 2004) and included age, BMI classes, sex, hypertensive status, physical inactivity and parental diabetes; diabetes was screened on the basis of fasting and/or 2-hour hyperglycaemia (WHO, 1999; The Expert Committee, 1997).

This analysis aims to answer a practical question: which of these three anthropometric parameters: BMI, waist circumference or WHR best identifies subjects who have diabetic levels of fasting plasma glucose or obesity-associated dyslipidaemia, and what are the appropriate corresponding thresholds. A second question is to compare the sensitivities of one simple anthropometric measure with the diabetes risk scores cited above for the selection of subjects who should be screened for diabetes.

## Subjects and methods

We analysed data from men and women, aged between 40 and 64 years, recruited in 1994-1996 from attendees at ten Health Examination Centres of the French Social Security in the central-west of France. In France, 85% of the population is covered by this form of Social Security, and they are able to have an in-depth health check-up every five years. Men and women were equally divided over five year age classes. We study firstly, screening for diabetes in the 3574 subjects who were not treated by drugs for diabetes, and secondly, screening for obesity-associated dyslipidaemia in the 3241 subjects who were not treated by drugs for dyslipidaemia. The study has ethical approval from the CCPPRB (Comite Consultatif de Protection des Personnes dans la Recherche Biomédicale) of Bîcetre and participants signed a statement of informed consent.

Subjects with a fasting plasma glucose concentration  $\geq 7.0$  mmol/l, were classified as having a diabetic fasting glucose concentration, according to the epidemiological definition of diabetes (WHO, 1999; The Expert Committee, 1997). Subjects with triglycerides  $\geq 2.3$  mmol/l and/or HDL-cholesterol  $< 0.9/1.1$  mmol/l (men/women) were classed as having obesity-associated dyslipidaemia according to the thresholds given for high and low values respectively by the National Cholesterol Education Program (Expert Panel, 2001).

Weight, height, waist circumference (smallest circumference between lower ribs and iliac crests) and hip circumference (greatest circumference between iliac crests and thighs) were measured by trained personnel, with subjects wearing undergarments only. Blood pressures and heart rate were measured after at least 5 minutes of rest, with subjects in a supine position. Fasting blood samples were analysed in one of three laboratories (Institut inter-Regional pour la Santé at La Riche, Health Examination Centre laboratories at Blois and Orleans); a quality control was maintained between laboratories. Glucose was assayed by the glucose-oxidase peroxydase method on a Technicon RA 1000 or on a Specific or a Delta from KONELAB; HDL-cholesterol used a phosphotungstic precipitation method, triglycerides an enzymatic Trinder method and both were assayed with a Technicon DAX24 or on a Specific or a Delta from KONELAB.

All subjects were asked about their personal and family medical history by an examining physician. They were considered to have diabetes or cardiovascular disease in their family if their parents, brothers, sisters or children had these conditions; a personal history of cardiovascular disease refers to a past myocardial infarction, angina or stroke. Women were asked whether they had

given birth to an infant weighing more than 4 kg. Smoking status, alcohol consumption (daily intake of beer, cider, wine and spirits) and physical activity (sporting activity, physical activity at work and at home) were obtained from a self-questionnaire.

## 5 Statistical analysis

Data are summarised by their mean (standard deviation) or percentage. Characteristics were compared between subjects with and without a diabetic fasting glucose concentration, and between subjects with and without an obesity-associated dyslipidaemia, using analysis of variance or logistic regression, and an interaction term with sex was included to test whether the relation was significantly different in the two sexes.

For the ADA diabetes risk test (ADA, 2000; Herman *et al*, 1995), the percentages of subjects with scores of 10 or above were calculated. The items and the associated scores to be added together are:  $\geq 65$  years (score=9), 45 to 65 years (5),  $< 65$  and little or no exercise (5), BMI  $\geq 27$  kg/m<sup>2</sup> (5), parent with diabetes (1), sister or brother with diabetes (1), woman with a baby weighing more than 9 pounds (4 kg) at birth (1). The diabetes risk score developed in the UK (Griffin *et al*, 2000) was calculated for our population and the 30% of subjects the most at risk were identified. This score adds: - 0.0879 if female, + 1.22 if treated by anti-hypertensive medications, + 2.191 if treated by steroids, + 0.063 times age in years, + 0.699 if BMI between 25.00 and 27.49 kg/m<sup>2</sup>, + 1.970 if BMI between 27.50 and 29.99 kg/m<sup>2</sup>, + 2.518 if BMI  $\geq 30$  kg/m<sup>2</sup>, + 0.728 if parent or sibling diabetic, + 0.753 if parent and sibling diabetic, - 0.218 if ex-smoker, + 0.855 if smoker. The Dutch score (Baan *et al*, 1999) which included variables available in our study, was used for subjects  $\geq 55$  years, and added: age per 5 year increment above 55 years (score=2 per increment), male (5), BMI  $\geq 30$  kg/m<sup>2</sup> (5), use of anti-hypertensive medications (4). Similarly the 30% the most at risk were identified. The Danish score (Glumer *et al*, 2004) was developed for men and women aged 30 to 60 years and summed the following scores, age (years) 45.0-49.9 (7), 50.0-54.9 (13),  $\geq 55.0$  (18), male sex (4), BMI 25.0-29.9 kg/m<sup>2</sup> (7),  $\geq 30.0$  kg/m<sup>2</sup> (15), known hypertension (10), physical inactivity in leisure-time (6), parent with diabetes (7). A score of 31 or more was proposed in the Danish study as the threshold for proposing a blood test to screen for diabetes (Glumer *et al*, 2004), and we have also used the cut-off corresponding to the 30% of subjects the most at risk.

Receiver operating characteristic (ROC) curves were drawn, and the areas under the ROC curves calculated, for BMI, waist circumference and WHR as possible pre-screening tests for both a

diabetic fasting glucose and an obesity-associated dyslipidaemia. The choice of thresholds for BMI, waist circumference and WHR were based on the premise that sensitivity was the most important factor and the thresholds were determined from the relation between the sensitivity and the percentage of the population requiring screening. The “optimal thresholds”, where the average of sensitivity and specificity is maximized, were also determined.

The distribution of differences in sensitivities of BMI, waist circumference and WHR, at the chosen threshold values, were estimated using the bootstrap re-sampling method (Efron *et al*, 1993) with 1000 bootstrap samples, and sample sizes equal to that of the populations studied. The means and standard deviations of these distributions were used to estimate the differences and the 95% confidence intervals between sensitivities for these anthropometric parameters, and the differences were tested using a Wald statistic.

All analyses used the SAS software, version 6.

## Results

In subjects not treated for diabetes, 11% of men and 10% of women were obese ( $BMI \geq 30 \text{ kg/m}^2$ ) and 47% and 26% respectively, were overweight ( $BMI: 25 \text{ to } 30 \text{ kg/m}^2$ ).

### Diabetes

Among the 3576 subjects not treated by drugs for diabetes, 53 (3%) men and 22 (1%) women had a diabetic fasting glucose (Table 1); they were, on average, two to three years older than non-diabetic men and women and had significantly higher BMI, waist and hip circumferences, WHR and more were treated for hypertension (all  $P < 0.001$ ); as well they had a higher heart rate ( $P < 0.002$ ), less physical activity ( $P < 0.04$ ) and more diabetes in the family ( $P < 0.01$ ). All factors showed the same trend in men and women, excepting for alcohol intake ( $P < 0.03$  for interaction), which was significantly higher in men with a diabetic fasting glucose ( $P < 0.01$ ), but lower in the women with a diabetic fasting glucose ( $P < 0.1$ ). Women, having had a baby weighing more than 4 kg were more likely to have a diabetic fasting glucose ( $P < 0.04$ ).

The ROC curves (Fig. 1) for these three anthropometric parameters differed little for men: BMI, waist circumference and WHR had areas under the curve of 75%, 72% and 76% respectively; for women, BMI had the smallest area under the curve: 66%, with waist circumference and WHR having

areas of 74% and 77%. The optimal thresholds, in men / women were 27 / 25 kg/m<sup>2</sup>, 97 / 85 cm, 0.95 / 0.83 for BMI, waist circumference and WHR (Table 2).

For all three measures, the sensitivity increased rapidly up until the more corpulent 30% or 40% of the population was screened and then increased much more slowly (Fig. 2, Table 2); for both men and women, and for screening between 20% and 60% of the population, BMI and waist circumference had higher sensitivities than WHR.

If the more corpulent 30% of the population were to be screened, for BMI this would correspond to those subjects with a BMI  $\geq$  27 / 26 kg/m<sup>2</sup> for men/women, respectively, with sensitivities of 77% / 77% (Table 2). The thresholds corresponding to a 30% screening using waist circumference were 96 / 83 cm for men and women (sensitivities 74% / 82%), and for WHR, 0.96 / 0.83 respectively (sensitivities 66% / 77%).

For men, the difference in sensitivity between the 30% the more corpulent according to BMI or according to waist circumference was 4% (95% confidence interval: -4 to 12;  $P < 0.3$ ), and for BMI and WHR 11% (-2 to 24;  $P < 0.09$ ). For women, the waist circumference had the highest sensitivity, and the differences with BMI and WHR were 4% (-25 to 33;  $P < 0.8$ ) and 4% (-15 to 23;  $P < 0.7$ ). Thus, there were no significant differences in sensitivity for these three parameters when screening the more corpulent 30%.

The sensitivities of the American Diabetes Association risk score (ADA, 2000; Herman *et al*, 1995) were 74% in men, 73% in women, with lower specificities (53%, 57%) (Table 1) and 49% of the population would be identified for a blood test. If the 30% of the population with the highest UK risk scores (Griffin *et al*, 2000) were tested for fasting glucose, in men there was a high sensitivity and specificity (83% and 60%), but the sensitivity was lower in women (55%) with a 91% specificity; the Dutch score (Baan *et al*, 1999), evaluated only for subjects 55 years and over, had sensitivities and specificities of 81% and 39% for men, 17% and 91% for women for those within the top 30% of risk. For the Danish score (Glumer *et al*, 2004) using the recommended score threshold of 31, only 15% of subjects would require a blood test, and the corresponding sensitivities for a diabetic fasting plasma glucose were low at 42% for men and 27% for women. Alternatively, if the 70<sup>th</sup> percentile of this score is used, the corresponding score is 25 and the sensitivities increased to 62% and 41% with specificities of 68% and 78%.

## Obesity-associated dyslipidaemia

Of the 3242 subjects not treated by drugs for lipid disorders, 185 (12%) men and 89 (5%) women had obesity-associated dyslipidaemia. Comparing those with and without dyslipidaemia, the men with dyslipidaemia were younger, the women older ( $P < 0.004$  for interaction) (Table 1). Subjects with dyslipidaemia had higher anthropometric measures and heart rate, more were hypertensive, more smoked (all  $P < 0.0001$ ), more were physically inactive ( $P < 0.02$ ), and they consumed more alcohol ( $P < 0.05$ ).

For men, the ROC curves for BMI, waist circumference and WHR were almost identical. In comparison to BMI, waist circumference had an area under the ROC curve 1% greater, WHR 3% lower (Fig. 1). For women, the BMI did not perform as well as either the waist circumference or the WHR, which had areas under the ROC curve 19% and 28% greater. These ROC curves had lower profiles, closer to the diagonal line than those for a diabetic fasting glucose, indicating a random predictive test. The optimal thresholds were 26 / 24 kg/m<sup>2</sup> for BMI, 91 / 81 cm for waist and 0.94 / 0.83 for WHR for men / women respectively (Table 4).

The sensitivity for the three anthropometric parameters increased almost linearly with the percentage of the population sampled, although it increased more slowly after the most corpulent 40% of the population had been screened (Fig. 2). Screening the more obese 30% of the population with a BMI  $\geq 27 / 26$  kg/m<sup>2</sup> (men / women), yielded sensitivities of only 56% / 54%. A 78% sensitivity was only attained when the 50% of the population with the highest BMI ( $\geq 25 / 24$  kg/m<sup>2</sup> respectively) was screened (Fig. 2, Table 4).

For men, BMI and waist circumference had similar sensitivities, higher than for WHR for a given percentage of the population screened (Fig. 2). For women, waist circumference and WHR had a similar sensitivity, but BMI had a 5% to 10% lower sensitivity depending on the percentage of the population screened.

If the more corpulent 30% of the population were screened, then the sensitivities, in men / women, were for BMI 56% / 54%, for waist circumference 54% / 65% and for WHR 49% / 67%. The corresponding specificities were all higher than 70%. For men, BMI had the highest sensitivity, but it was not significantly higher than either the waist circumference: 2% (-4 to 7;  $P < 0.5$ ) or the WHR: 6% (-2 to 14;  $P < 0.16$ ). For women, the WHR had the highest sensitivity, but again it was not

significantly higher than that for the BMI: 8% (-3 to 20;  $P < 0.13$ ) or for the waist circumference: 2% (-6 to 11;  $P < 0.6$ ).

## Discussion

5 When the 30% more corpulent men and women from this French population were screened, there were no significant differences between the sensitivities of the three anthropometric measures (BMI, waist circumference and WHR) for a fasting diabetic glucose or for obesity-associated dyslipidaemia. All three measures showed better sensitivities for predicting a diabetic fasting glucose than for dyslipidaemia.

10 In comparison with diabetes risk scores, screening the 30% more corpulent using the BMI gave better sensitivity than the American Diabetes Association risk score with fewer subjects requiring screening (ADA, 2000; Herman *et al*, 1995) and better sensitivity than the Danish score (Glumer *et al*, 2004). For the UK risk score (Griffin *et al*, 2000) and the Dutch score (Baan *et al*, 1999) the sensitivity was a little higher for men, lower for women. The obesity indices performed well in this French  
15 population, and are simple for clinical practice. Diabetes risk scores rely on both the exact wording of the questions and the cultural background and the Dutch score performed very poorly in French women.

Our study is limited by the number of subjects with the studied abnormalities, but given the level of non-significance of the results, it is unlikely that they would differ if the study population was  
20 larger. The age range of 40 to 64 years is also limited, but is an appropriate age range for the screening of metabolic abnormalities because their prevalences are not low, but there is still time for effective treatment for the prevention of complications. The subjects studied in this report are from the 85% of the French population covered by this form of French Social Security; they were invited and accepted the invitation to have a periodic health check up and agreed to participate in a cohort study.  
25 They are probably representative of health conscious subjects who would present for screening – screening is rarely taken up universally by all of a population. Our results rely on the consensus definition for a diabetic fasting glucose (WHO, 1999; ADA, 1997). There is no consensus definition for the dyslipidaemia associated with obesity, a dyslipidaemia associated with the metabolic syndrome. We have taken the thresholds for triglycerides and for HDL-cholesterol from the National Cholesterol  
30 Education Program definitions of the metabolic syndrome (Expert Panel, 2001).

The traditional way to evaluate screening tests is to draw ROC curves and to compare the areas under these curves. However, these curves are of interest over a small central range of thresholds, thus it is debatable whether it is useful to compare, with statistical tests, the area under the curve for different screening parameters. Often, an “optimal threshold” is defined, which maximises the (sensitivity + specificity). Again, this is not always appropriate in cases such as ours, where the sensitivity is of paramount importance, the specificity of much less importance. This choice of sensitivity as a key parameter is corroborated by recent articles indicating that screening for diabetes does not impact on the quality of life nor have a psychological impact (Adriaanse *et al*, 2002; Edelman *et al*, 2002), and we have based our criteria on maximising sensitivity, for a given percentage of the population to be screened. As commented by Wareham and Griffin (2001), it is hard to justify screening an entire population, but targeting sub-groups may be justified. In this study population we recommend screening the more corpulent 30% of the population because the sensitivity increases very little when a higher percentage of subjects are screened; in other situations where these conditions are more frequent, a higher percentage may need to be screened.

While it is well established that there is a stronger relation between cardiovascular risk and central adiposity than with BMI (Larsson *et al*, 1984; Lapidus *et al*, 1984), the waist circumference is not habitually measured in clinical practice. These measures are time consuming, they have to be done in addition to the usual clinical examination. However, the waist circumference may be of more interest in patient care, as patients are more readily aware of an increasing waistline than an increasing weight. BMI and waist circumference are very highly correlated: in the pooled data of 19 populations from the WHO MONICA project, BMI explained 77% of the variance of the waist circumference in men and 75% in women (Molarius *et al*, 1998). The waist circumference has a higher measurement error than the BMI, especially in the obese (Nordhamm *et al*, 2000), and this might be why the theoretical advantage of waist circumference over BMI for screening metabolic abnormalities, did not translate into a practical advantage.

Two studies with very similar methodology have been reported in Hong Kong Chinese and in a Mexican population (Ko *et al*, 1999; Berber *et al*, 2001). Both use anthropometric measures to screen for diabetes and dyslipidaemia, the latter had a more liberal definition than in our study. The “optimal thresholds” were determined, but from the data given it is unlikely that their performances differed significantly. In the Baltimore Longitudinal Study of Aging, the waist circumference added little

over the BMI in the prediction of the level of cardiovascular risk factors (Iwao *et al*, 2001). Another recent article comes from the NHANES III study (Zhu *et al*, 2002) and it used the criteria of at least one of four cardiovascular risk factors. The corresponding “optimal thresholds” for BMI were 25 / 26 kg/m<sup>2</sup> in men / women, and 96 / 86 cm for the waist circumference. The sensitivities were similar for BMI and waist in men, but in women, the waist had higher sensitivity than the BMI. Again no comparative statistical tests were given.

While there are commonly agreed thresholds for BMI, a number of different thresholds have been given in the literature for both waist circumference and WHR. Indeed, in the definitions of the metabolic syndrome (Expert Panel, 2001; WHO, 1999), the limits used are WHR  $\geq$  0.90 / 0.85 or waist circumference > 102 / 88 cm, and no justifications were given. The World Health Organisation Consultation on Obesity (WHO, 1999) suggested that the commonly used WHR threshold for defining abdominal fat accumulation is 1.0/0.85 in men/women. For waist circumference they cited two thresholds of 94 and 102 cm in men, 80 and 88 cm in women. These thresholds were developed from Scottish data on the basis of other anthropometric parameters, namely BMI  $\geq$  25 or 30 kg/m<sup>2</sup> and a WHR  $\geq$  0.95 / 0.80 (men / women) (Lean *et al*, 1995). These particular thresholds have also been studied in a Dutch population in relation with metabolic abnormalities but while there was a linear relation between waist circumference and these abnormalities, no specific threshold for waist circumference was evident (Han *et al*, 1995). One of the first to document a threshold for waist circumference was Poulriot (Poulriot *et al*, 1994) in relation with the volume of visceral fat, and the threshold was 100 cm.

Consideration may need to be made for age, gender, ethnic group and the disease being studied and there is still need for “consistency ... more scientifically and theoretically solid basis for the selection and use of anthropometric indicators of abdominal obesity and cut-offs ...” (Molarius *et al*, 1998). The International Diabetes Federation 2005 Consensus definition of the metabolic syndrome uses ethnic-specific cut-points for waist circumference, (94 / 80 cm in European men / women), and comment is made that they are “pragmatic cut-points ... better data will be needed to link these to risk” (IDF, 2005).

From our French data of men and women aged 40 to 64 years, presenting for a health screening, we would suggest that the more obese 30% of the population be screened. As there is no difference between BMI, waist circumference and WHR in screening for diabetes and obesity-

associated dyslipidaemia, the most convenient measure should be used. Current medical practice is to assess the BMI. When BMI  $\geq 27$  kg/m<sup>2</sup> for men and  $\geq 26$  kg/m<sup>2</sup> for women, screening for diabetes and obesity-associated dyslipidaemia is recommended. Alternatively, for the waist circumference which requires only one measure, the recommended thresholds are  $\geq 96$  cm in men and  $\geq 83$  cm in women. Similar analyses are required in other populations to compare the thresholds for both BMI and waist circumference.

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## TITLES AND LEGENDS TO FIGURES

- 5 **Figure 1**—Receiver Operating Characteristic (ROC) curves for men and women for a diabetic fasting plasma glucose ( $\geq 7.0$  mmol/l) (A and C) and for an obesity-associated dyslipidaemia (triglycerides  $\geq 2.3$  mmol/l and/or HDL-cholesterol  $< 0.9/1.1$  mmol/l (men/women)) (B and D respectively) using the BMI, the waist circumference and the waist hip ratio. The men and women were aged 40 to 64 years; for the diabetes analysis, subjects were not treated for diabetes; for the obesity-associated dyslipidaemia analysis, subjects were not treated for dyslipidaemia. The D.E.S.I.R. Study.
- 10 **Figure 2**—Sensitivity for a diabetic fasting glucose ( $\geq 7.0$  mmol/l) (A and C men and women respectively) and for obesity-associated dyslipidaemia (triglycerides  $\geq 2.3$  mmol/l and/or HDL-cholesterol  $< 0.9/1.1$  mmol/l (men/women)) (B and D) for various percentages of the population screened, according to BMI, waist circumference and waist hip ratio. The men and women were aged 40 to 64 years; for the diabetes analysis, subjects were not treated for diabetes; for the obesity associated dyslipidaemia analysis, subject, were not treated for dyslipidaemia. The D.E.S.I.R. Study.
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