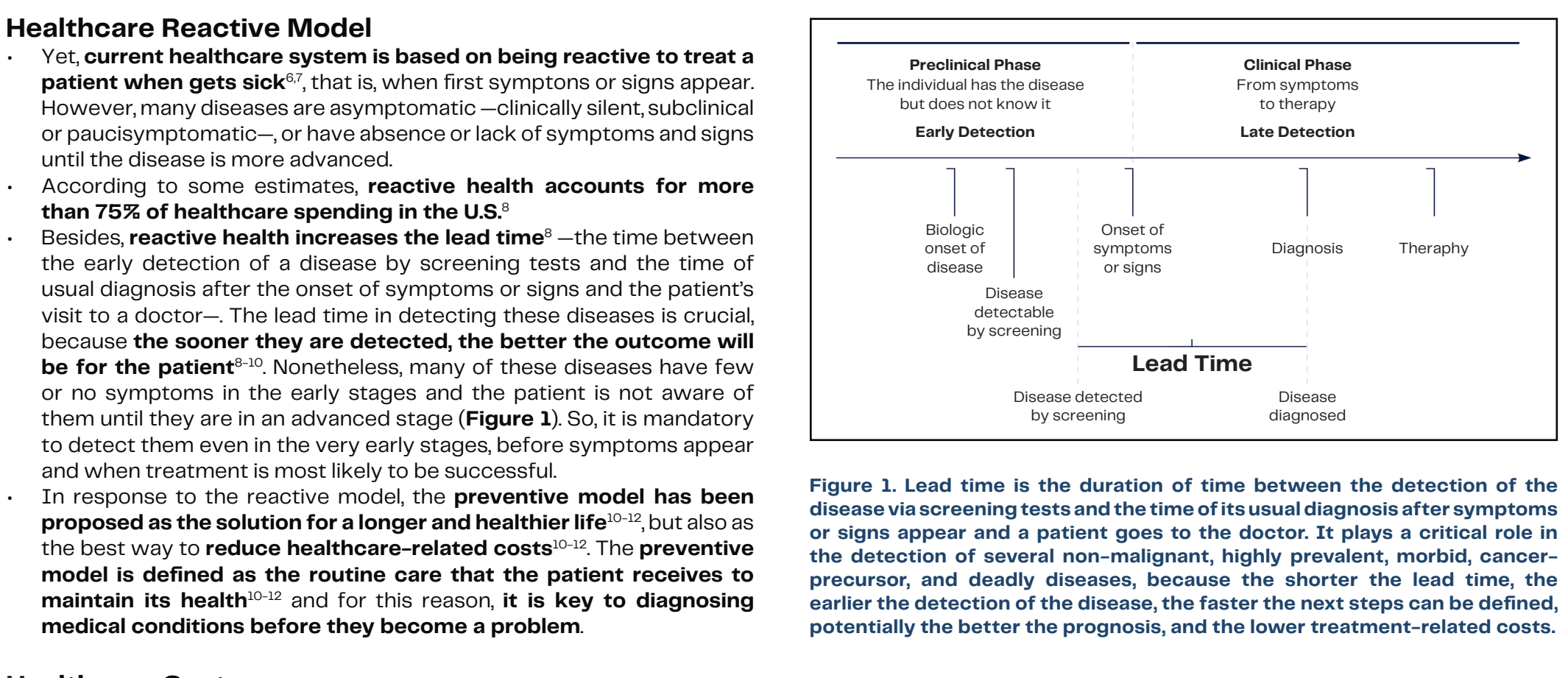


**Authors:** Sergio J. Calleja<sup>1</sup>, Adrià Roca<sup>2</sup>, José D. Santoribio<sup>3</sup>  
**Affiliations:** <sup>1</sup>Kience, Wilmington, U.S.; <sup>2</sup>Blueberry Diagnostics, Barcelona, Spain; <sup>3</sup>Hospital Universitario Puerto Real, Cádiz, Spain

### BACKGROUND

According to the National Center for Health Statistics (NCHS), there are many diseases whose prevalence is highly concerning. Some are related to the pancreatic endocrine function, and the number of cases of these diseases is extremely high and it is predicted to continue increasing in the next years. For this reason, they are frequently listed among the most morbid diseases worldwide. Although they are not life-threatening, they can predispose patients to develop more severe conditions if they are not detected or treated at an early stage.  
Overweight and obesity, along with metabolic syndrome (MetS) are the main risk factors for these diseases.  
There are 2 billion people worldwide with overweight or obesity—including 124 million children—and these figures are expected to continue to increase. As a consequence, the prevalence of pancreatic endocrine diseases—such as insulin resistance (IR), prediabetes, and type 2 diabetes mellitus (DM2)—has become a serious global concern.



Reactive model: Patient with disease → Diagnosis → Therapy. This model is reactive to a patient when they get sick, that is, when first symptoms or signs appear. However, many diseases are asymptomatic—clinically silent, subclinical or paucisymptomatic—so they do not have obvious or lack of symptoms and signs until the disease is more advanced.

### Healthcare Costs

The high cost of healthcare is a burden on U.S. families<sup>10</sup>. About half of U.S. adults say it is difficult to afford healthcare costs<sup>10,11</sup>, and one in four say they or a family member in their household had problems paying for healthcare in the past 12 months<sup>10</sup>. Younger adults, those with lower incomes, adults in fair or poor health, and the uninsured are particularly likely to report problems affording healthcare in the last year.  
The cost of healthcare can lead some to put off needed care<sup>10,11</sup>—one in four adults says that in the past 12 months they have skipped or postponed getting healthcare they needed because of the cost.  
Notable in tenured adults (51%) say they would not need care because of the cost.  
Healthcare debt is a burden for a large share of Americans—about four in ten adults (41%) report having debt due to medical or dental bills including debts owed to credit cards, collections agencies, family and friends, banks, and other lenders to pay for their healthcare costs—with disproportionate shares of Black and Hispanic adults, women, patients, and those with low incomes, and uninsured adults saying they have healthcare debt<sup>10</sup>.

### Chronic, Morbid and Cancer-Preventor Diseases, and Aging

The World Health Organization (WHO) estimates that chronic illnesses account for half of the global disease burden<sup>12</sup>, a figure that will rise as the world's population ages. Chronic diseases pose a unique challenge as they frequently are undiagnosed, often undetected, and incurable. They are continuous and often caused by specific and preventable health risks.  
On the other hand, long waiting lists exacerbated by the pandemic and new cases being treated further and further down the line<sup>13</sup>. At the same time, we are seeing a consistent rise in chronic illnesses—such as cardiovascular disease, diabetes, and cancer. Moreover, the risk of these chronic diseases actually increases with age as nearly 95% of adults 60 and older have at least one—while nearly 80% have two or more<sup>14</sup>. With an ageing population and these growing numbers, it is clear this model is not sustainable<sup>15</sup>.

### OBJECTIVES

To define a minimum blood and/or urine—panel capable of confirming—and/or detecting—the main pancreatic endocrine diseases—insulin resistance (HOMA-IR), HOMA-Beta, HOMA-A, HOMA-2, and the quantitative insulin-sensitivity check index (QUICKI)—as well as establishing the 7.5-year risk of developing DM2 (DM2-7.5). If achieved, we see it is also able to detect any possible alteration related with these diseases, such as cardiovascular affections—such as cardiovascular disease (CVD), atherosclerotic cardiovascular disease (ASCVD), and myocardial infarction (MI)—and chronic kidney disease (CKD). In this process the price should be a very important variable in this panel, so that the cheapest one to enable universal and quality access to healthcare.  
To validate whether this new approach to a Evidence-Based Laboratory Medicine (EBLM) routine blood and/or urine—if needed—could be used as a non-invasive test to assist doctors in the assessment—as well as screening—of the main pancreatic endocrine diseases, such as insulin resistance (IR), prediabetes, diabetes mellitus (DM2), and renal function diseases. The related costs and additional information—such as patient information, and other health information—will be used to help the medical community to understand how EBLM and new technologies—mainly machine learning (ML) algorithms (also known as AI-powered diagnostic tools) based in large and quality datasets—can help healthcare professionals to improve diagnosis accuracy, reduce medical errors and misdiagnoses, and avoid unnecessary—and/or unnecessary—tests.  
To fine-tune the final details of our algorithm as a preliminary step to the upcoming multicenter and international clinical trial of 26,000 patients that will be performed from March 2025 to December 2026 (we are still in the process of recruiting hospitals and medical centers).  
To validate the performance and accuracy of the algorithm when used with vendors other than those with which the original algorithms were developed—Synnex (Kobe, Japan) for hematology and Roche Diagnostics (Rochevex, Switzerland) for biochemistry and immunoassay—, since several previous correlation studies alerted about potentially moderate differences in the performance between different reagent vendors—mainly in the normality limit.  
To collect data for future mid- and/or long-term studies related to health economics outcome research (HEOR)<sup>16</sup> to analyze the cost effectiveness of machine learning (ML) algorithms as a CDS.

### METHODS

This study was developed as a part of a previous one that had been presented at the European Society of Medical Oncology (ESMO) Congress 2024 for Multi-Cancer Early Detection (MCEd)<sup>17</sup>. From this previous study—with 90 routine laboratory determinations included (Table 3)—, new studies were conducted, such as the one described here.

In this way, on the one hand, to develop the original algorithm for an innovative evidence-based laboratory medicine (EBLM) test to assist doctors in the assessment of pancreatic endocrine function, and on the other hand, to validate the performance and accuracy of the algorithm when used with vendors other than those with which the original algorithms were developed—Synnex (Kobe, Japan) for hematology and Roche Diagnostics (Rochevex, Switzerland) for biochemistry and immunoassay—, since several previous correlation studies alerted about potentially moderate differences in the performance between different reagent vendors—mainly in the normality limit.

First, the statistical evaluation of the algorithm was performed following the next steps:

- The initial sample—training set of 9,301 patients—was divided in the training and validation sets (80% of the total patients for the training set and the remaining 20% for the validation set), to determine an initial accuracy.
- All the data was pre-processed by converting those numerical variables that were categorical.
- The next step consisted in visualizing the categorical dependent variables and all the different qualitative variables, to verify if the distribution was balanced or not, and if necessary, a corrective method was applied to adjust the unbalance of the classes, by modifying the original size of the whole training data.
- The absent cases were detected, and an imputation method was implemented, either with the median or not, or with the frequent values.
- All the training and validation sets were analyzed, to detect variables with a variance of zero or close, because their variability will be similar or very low and they will not be useful.
- The statistical variables (outliers) that can affect the distribution of the variables were detected in the quantitative variables of the training set, to apply corrective measures and, if very small values were found, the imputation of arbitrary values was studied, determining firstly the cut-off value that indicates the beginning of the variable, and the median was used as a replacement value for those observations that were above the cut-off.
- The initial binary logistic regression (logit) was estimated by the general linear model (GLM) algorithm, with the argument family = binomial (link = logit) because the dependent variable is binary categorical, and the threshold to classify the attribute depended on what we wanted to predict (prior the cut-off point was 0.5, because it is the standard cut-off to classify as healthy and sick).
- The logit model achieved was evaluated through the following methods: assessment of the influential values and possibly atypical from the residues of the logit model; multicollinearity analysis—to evaluate the presence and the magnitude of strong linear relationships between predictor variables (dependent variables) in the model; goodness of fit to determine if the model is adequate for its use; decision making or in making predictions—calculation of the importance of the predictive variables in the model, considering their weight through the derivation of the mean average precision and the Gini decreasing average; as well as the final validation for the model with the validation set of the 20% to determine the sensitivity, specificity, area under the receiver operating characteristic (AUROC) curve, positive predictive value (PPV), and negative predictive value (NPV).
- The cut-off point was optimized, to finally adjust the binary logistic regression model.
- The final evaluation of the binary logistic regression model was performed with the optimal cut-off point.

Second, several combinations—up to 1 x 10<sup>10</sup>—were performed to find most significant groupings of laboratory determinations—mainly for the pancreatic endocrine function, but also for all other body functions and systems involved and/or related with them, this is, both causes and/or consequences—.

Third, several calculations were performed, mainly those related with atherogenic indices (Table 5). In this way, atherogenic endocrine indices (Table 5), and renal indices (Table 5). We also performed the assessment of the pancreatic endocrine function (EBLM) in this way, performed atherogenic index and cardiovascular causes were atherogenic indices (ACI)<sup>18</sup>, atherogenic index of plasma (AIP)<sup>19</sup>, atherogenic index I (CRI-I)<sup>20</sup>, CRI-II<sup>21</sup>, fibrinogen<sup>22</sup>, fibrinogen<sup>23</sup>, fibrinogen<sup>24</sup>, fibrinogen<sup>25</sup>, fibrinogen<sup>26</sup>, fibrinogen<sup>27</sup>, fibrinogen<sup>28</sup>, fibrinogen<sup>29</sup>, fibrinogen<sup>30</sup>, fibrinogen<sup>31</sup>, fibrinogen<sup>32</sup>, fibrinogen<sup>33</sup>, fibrinogen<sup>34</sup>, fibrinogen<sup>35</sup>, fibrinogen<sup>36</sup>, fibrinogen<sup>37</sup>, fibrinogen<sup>38</sup>, fibrinogen<sup>39</sup>, fibrinogen<sup>40</sup>, fibrinogen<sup>41</sup>, fibrinogen<sup>42</sup>, fibrinogen<sup>43</sup>, fibrinogen<sup>44</sup>, fibrinogen<sup>45</sup>, fibrinogen<sup>46</sup>, fibrinogen<sup>47</sup>, fibrinogen<sup>48</sup>, fibrinogen<sup>49</sup>, fibrinogen<sup>50</sup>, fibrinogen<sup>51</sup>, fibrinogen<sup>52</sup>, fibrinogen<sup>53</sup>, fibrinogen<sup>54</sup>, fibrinogen<sup>55</sup>, fibrinogen<sup>56</sup>, fibrinogen<sup>57</sup>, fibrinogen<sup>58</sup>, fibrinogen<sup>59</sup>, fibrinogen<sup>60</sup>, fibrinogen<sup>61</sup>, fibrinogen<sup>62</sup>, fibrinogen<sup>63</sup>, fibrinogen<sup>64</sup>, fibrinogen<sup>65</sup>, fibrinogen<sup>66</sup>, fibrinogen<sup>67</sup>, fibrinogen<sup>68</sup>, fibrinogen<sup>69</sup>, fibrinogen<sup>70</sup>, fibrinogen<sup>71</sup>, fibrinogen<sup>72</sup>, fibrinogen<sup>73</sup>, fibrinogen<sup>74</sup>, fibrinogen<sup>75</sup>, fibrinogen<sup>76</sup>, fibrinogen<sup>77</sup>, fibrinogen<sup>78</sup>, fibrinogen<sup>79</sup>, fibrinogen<sup>80</sup>, fibrinogen<sup>81</sup>, fibrinogen<sup>82</sup>, fibrinogen<sup>83</sup>, fibrinogen<sup>84</sup>, fibrinogen<sup>85</sup>, fibrinogen<sup>86</sup>, fibrinogen<sup>87</sup>, fibrinogen<sup>88</sup>, fibrinogen<sup>89</sup>, fibrinogen<sup>90</sup>, fibrinogen<sup>91</sup>, fibrinogen<sup>92</sup>, fibrinogen<sup>93</sup>, fibrinogen<sup>94</sup>, fibrinogen<sup>95</sup>, fibrinogen<sup>96</sup>, fibrinogen<sup>97</sup>, fibrinogen<sup>98</sup>, fibrinogen<sup>99</sup>, fibrinogen<sup>100</sup>, fibrinogen<sup>101</sup>, fibrinogen<sup>102</sup>, fibrinogen<sup>103</sup>, fibrinogen<sup>104</sup>, fibrinogen<sup>105</sup>, fibrinogen<sup>106</sup>, fibrinogen<sup>107</sup>, fibrinogen<sup>108</sup>, fibrinogen<sup>109</sup>, fibrinogen<sup>110</sup>, fibrinogen<sup>111</sup>, fibrinogen<sup>112</sup>, fibrinogen<sup>113</sup>, fibrinogen<sup>114</sup>, fibrinogen<sup>115</sup>, fibrinogen<sup>116</sup>, fibrinogen<sup>117</sup>, fibrinogen<sup>118</sup>, fibrinogen<sup>119</sup>, fibrinogen<sup>120</sup>, fibrinogen<sup>121</sup>, fibrinogen<sup>122</sup>, fibrinogen<sup>123</sup>, fibrinogen<sup>124</sup>, fibrinogen<sup>125</sup>, fibrinogen<sup>126</sup>, fibrinogen<sup>127</sup>, fibrinogen<sup>128</sup>, fibrinogen<sup>129</sup>, fibrinogen<sup>130</sup>, fibrinogen<sup>131</sup>, fibrinogen<sup>132</sup>, fibrinogen<sup>133</sup>, fibrinogen<sup>134</sup>, fibrinogen<sup>135</sup>, fibrinogen<sup>136</sup>, fibrinogen<sup>137</sup>, fibrinogen<sup>138</sup>, fibrinogen<sup>139</sup>, fibrinogen<sup>140</sup>, fibrinogen<sup>141</sup>, fibrinogen<sup>142</sup>, fibrinogen<sup>143</sup>, fibrinogen<sup>144</sup>, fibrinogen<sup>145</sup>, fibrinogen<sup>146</sup>, fibrinogen<sup>147</sup>, fibrinogen<sup>148</sup>, fibrinogen<sup>149</sup>, fibrinogen<sup>150</sup>, fibrinogen<sup>151</sup>, fibrinogen<sup>152</sup>, fibrinogen<sup>153</sup>, fibrinogen<sup>154</sup>, fibrinogen<sup>155</sup>, fibrinogen<sup>156</sup>, fibrinogen<sup>157</sup>, fibrinogen<sup>158</sup>, fibrinogen<sup>159</sup>, fibrinogen<sup>160</sup>, fibrinogen<sup>161</sup>, fibrinogen<sup>162</sup>, fibrinogen<sup>163</sup>, fibrinogen<sup>164</sup>, fibrinogen<sup>165</sup>, fibrinogen<sup>166</sup>, fibrinogen<sup>167</sup>, fibrinogen<sup>168</sup>, fibrinogen<sup>169</sup>, fibrinogen<sup>170</sup>, fibrinogen<sup>171</sup>, fibrinogen<sup>172</sup>, fibrinogen<sup>173</sup>, fibrinogen<sup>174</sup>, fibrinogen<sup>175</sup>, fibrinogen<sup>176</sup>, fibrinogen<sup>177</sup>, fibrinogen<sup>178</sup>, fibrinogen<sup>179</sup>, fibrinogen<sup>180</sup>, fibrinogen<sup>181</sup>, fibrinogen<sup>182</sup>, fibrinogen<sup>183</sup>, fibrinogen<sup>184</sup>, fibrinogen<sup>185</sup>, fibrinogen<sup>186</sup>, fibrinogen<sup>187</sup>, fibrinogen<sup>188</sup>, fibrinogen<sup>189</sup>, fibrinogen<sup>190</sup>, fibrinogen<sup>191</sup>, fibrinogen<sup>192</sup>, fibrinogen<sup>193</sup>, fibrinogen<sup>194</sup>, fibrinogen<sup>195</sup>, fibrinogen<sup>196</sup>, fibrinogen<sup>197</sup>, fibrinogen<sup>198</sup>, fibrinogen<sup>199</sup>, fibrinogen<sup>200</sup>, fibrinogen<sup>201</sup>, fibrinogen<sup>202</sup>, fibrinogen<sup>203</sup>, fibrinogen<sup>204</sup>, fibrinogen<sup>205</sup>, fibrinogen<sup>206</sup>, fibrinogen<sup>207</sup>, fibrinogen<sup>208</sup>, fibrinogen<sup>209</sup>, fibrinogen<sup>210</sup>, fibrinogen<sup>211</sup>, fibrinogen<sup>212</sup>, fibrinogen<sup>213</sup>, fibrinogen<sup>214</sup>, fibrinogen<sup>215</sup>, fibrinogen<sup>216</sup>, fibrinogen<sup>217</sup>, fibrinogen<sup>218</sup>, fibrinogen<sup>219</sup>, fibrinogen<sup>220</sup>, fibrinogen<sup>221</sup>, fibrinogen<sup>222</sup>, fibrinogen<sup>223</sup>, fibrinogen<sup>224</sup>, fibrinogen<sup>225</sup>, fibrinogen<sup>226</sup>, fibrinogen<sup>227</sup>, fibrinogen<sup>228</sup>, fibrinogen<sup>229</sup>, fibrinogen<sup>230</sup>, fibrinogen<sup>231</sup>, fibrinogen<sup>232</sup>, fibrinogen<sup>233</sup>, fibrinogen<sup>234</sup>, fibrinogen<sup>235</sup>, fibrinogen<sup>236</sup>, fibrinogen<sup>237</sup>, fibrinogen<sup>238</sup>, fibrinogen<sup>239</sup>, fibrinogen<sup>240</sup>, fibrinogen<sup>241</sup>, fibrinogen<sup>242</sup>, fibrinogen<sup>243</sup>, fibrinogen<sup>244</sup>, fibrinogen<sup>245</sup>, fibrinogen<sup>246</sup>, fibrinogen<sup>247</sup>, fibrinogen<sup>248</sup>, fibrinogen<sup>249</sup>, fibrinogen<sup>250</sup>, fibrinogen<sup>251</sup>, fibrinogen<sup>252</sup>, fibrinogen<sup>253</sup>, fibrinogen<sup>254</sup>, fibrinogen<sup>255</sup>, fibrinogen<sup>256</sup>, fibrinogen<sup>257</sup>, fibrinogen<sup>258</sup>, fibrinogen<sup>259</sup>, fibrinogen<sup>260</sup>, fibrinogen<sup>261</sup>, fibrinogen<sup>262</sup>, fibrinogen<sup>263</sup>, fibrinogen<sup>264</sup>, fibrinogen<sup>265</sup>, fibrinogen<sup>266</sup>, fibrinogen<sup>267</sup>, fibrinogen<sup>268</sup>, fibrinogen<sup>269</sup>, fibrinogen<sup>270</sup>, fibrinogen<sup>271</sup>, fibrinogen<sup>272</sup>, fibrinogen<sup>273</sup>, fibrinogen<sup>274</sup>, fibrinogen<sup>275</sup>, fibrinogen<sup>276</sup>, fibrinogen<sup>277</sup>, fibrinogen<sup>278</sup>, fibrinogen<sup>279</sup>, fibrinogen<sup>280</sup>, fibrinogen<sup>281</sup>, fibrinogen<sup>282</sup>, fibrinogen<sup>283</sup>, fibrinogen<sup>284</sup>, fibrinogen<sup>285</sup>, fibrinogen<sup>286</sup>, fibrinogen<sup>287</sup>, fibrinogen<sup>288</sup>, fibrinogen<sup>289</sup>, fibrinogen<sup>290</sup>, fibrinogen<sup>291</sup>, fibrinogen<sup>292</sup>, fibrinogen<sup>293</sup>, fibrinogen<sup>294</sup>, fibrinogen<sup>295</sup>, fibrinogen<sup>296</sup>, fibrinogen<sup>297</sup>, fibrinogen<sup>298</sup>, fibrinogen<sup>299</sup>, fibrinogen<sup>300</sup>, fibrinogen<sup>301</sup>, fibrinogen<sup>302</sup>, fibrinogen<sup>303</sup>, fibrinogen<sup>304</sup>, fibrinogen<sup>305</sup>, fibrinogen<sup>306</sup>, fibrinogen<sup>307</sup>, fibrinogen<sup>308</sup>, fibrinogen<sup>309</sup>, fibrinogen<sup>310</sup>, fibrinogen<sup>311</sup>, fibrinogen<sup>312</sup>, fibrinogen<sup>313</sup>, fibrinogen<sup>314</sup>, fibrinogen<sup>315</sup>, fibrinogen<sup>316</sup>, fibrinogen<sup>317</sup>, fibrinogen<sup>318</sup>, fibrinogen<sup>319</sup>, fibrinogen<sup>320</sup>, fibrinogen<sup>321</sup>, fibrinogen<sup>322</sup>, fibrinogen<sup>323</sup>, fibrinogen<sup>324</sup>, fibrinogen<sup>325</sup>, fibrinogen<sup>326</sup>, fibrinogen<sup>327</sup>, fibrinogen<sup>328</sup>, fibrinogen<sup>329</sup>, fibrinogen<sup>330</sup>, fibrinogen<sup>331</sup>, fibrinogen<sup>332</sup>, fibrinogen<sup>333</sup>, fibrinogen<sup>334</sup>, fibrinogen<sup>335</sup>, fibrinogen<sup>336</sup>, fibrinogen<sup>337</sup>, fibrinogen<sup>338</sup>, fibrinogen<sup>339</sup>, fibrinogen<sup>340</sup>, fibrinogen<sup>341</sup>, fibrinogen<sup>342</sup>, fibrinogen<sup>343</sup>, fibrinogen<sup>344</sup>, fibrinogen<sup>345</sup>, fibrinogen<sup>346</sup>, fibrinogen<sup>347</sup>, fibrinogen<sup>348</sup>, fibrinogen<sup>349</sup>, fibrinogen<sup>350</sup>, fibrinogen<sup>351</sup>, fibrinogen<sup>352</sup>, fibrinogen<sup>353</sup>, fibrinogen<sup>354</sup>, fibrinogen<sup>355</sup>, fibrinogen<sup>356</sup>, fibrinogen<sup>357</sup>, fibrinogen<sup>358</sup>, fibrinogen<sup>359</sup>, fibrinogen<sup>360</sup>, fibrinogen<sup>361</sup>, fibrinogen<sup>362</sup>, fibrinogen<sup>363</sup>, fibrinogen<sup>364</sup>, fibrinogen<sup>365</sup>, fibrinogen<sup>366</sup>, fibrinogen<sup>367</sup>, fibrinogen<sup>368</sup>, fibrinogen<sup>369</sup>, fibrinogen<sup>370</sup>, fibrinogen<sup>371</sup>, fibrinogen<sup>372</sup>, fibrinogen<sup>373</sup>, fibrinogen<sup>374</sup>, fibrinogen<sup>375</sup>, fibrinogen<sup>376</sup>, fibrinogen<sup>377</sup>, fibrinogen<sup>378</sup>, fibrinogen<sup>379</sup>, fibrinogen<sup>380</sup>, fibrinogen<sup>381</sup>, fibrinogen<sup>382</sup>, fibrinogen<sup>383</sup>, fibrinogen<sup>384</sup>, fibrinogen<sup>385</sup>, fibrinogen<sup>386</sup>, fibrinogen<sup>387</sup>, fibrinogen<sup>388</sup>, fibrinogen<sup>389</sup>, fibrinogen<sup>390</sup>, fibrinogen<sup>391</sup>, fibrinogen<sup>392</sup>, fibrinogen<sup>393</sup>, fibrinogen<sup>394</sup>, fibrinogen<sup>395</sup>, fibrinogen<sup>396</sup>, fibrinogen<sup>397</sup>, fibrinogen<sup>398</sup>, fibrinogen<sup>399</sup>, fibrinogen<sup>400</sup>, fibrinogen<sup>401</sup>, fibrinogen<sup>402</sup>, fibrinogen<sup>403</sup>, fibrinogen<sup>404</sup>, fibrinogen<sup>405</sup>, fibrinogen<sup>406</sup>, fibrinogen<sup>407</sup>, fibrinogen<sup>408</sup>, fibrinogen<sup>409</sup>, fibrinogen<sup>410</sup>, fibrinogen<sup>411</sup>, fibrinogen<sup>412</sup>, fibrinogen<sup>413</sup>, fibrinogen<sup>414</sup>, fibrinogen<sup>415</sup>, fibrinogen<sup>416</sup>, fibrinogen<sup>417</sup>, fibrinogen<sup>418</sup>, fibrinogen<sup>419</sup>, fibrinogen<sup>420</sup>, fibrinogen<sup>421</sup>, fibrinogen<sup>422</sup>, fibrinogen<sup>423</sup>, fibrinogen<sup>424</sup>, fibrinogen<sup>425</sup>, fibrinogen<sup>426</sup>, fibrinogen<sup>427</sup>, fibrinogen<sup>428</sup>, fibrinogen<sup>429</sup>, fibrinogen<sup>430</sup>, fibrinogen<sup>431</sup>, fibrinogen<sup>432</sup>, fibrinogen<sup>433</sup>, fibrinogen<sup>434</sup>, fibrinogen<sup>435</sup>, fibrinogen<sup>436</sup>, fibrinogen<sup>437</sup>, fibrinogen<sup>438</sup>, fibrinogen<sup>439</sup>, fibrinogen<sup>440</sup>, fibrinogen<sup>441</sup>, fibrinogen<sup>442</sup>, fibrinogen<sup>443</sup>, fibrinogen<sup>444</sup>, fibrinogen<sup>445</sup>, fibrinogen<sup>446</sup>, fibrinogen<sup>447</sup>, fibrinogen<sup>448</sup>, fibrinogen<sup>449</sup>, fibrinogen<sup>450</sup>, fibrinogen<sup>451</sup>, fibrinogen<sup>452</sup>, fibrinogen<sup>453</sup>, fibrinogen<sup>454</sup>, fibrinogen<sup>455</sup>, fibrinogen<sup>456</sup>, fibrinogen<sup>457</sup>, fibrinogen<sup>458</sup>, fibrinogen<sup>459</sup>, fibrinogen<sup>460</sup>, fibrinogen<sup>461</sup>, fibrinogen<sup>462</sup>, fibrinogen<sup>463</sup>, fibrinogen<sup>464</sup>, fibrinogen<sup>465</sup>, fibrinogen<sup>466</sup>, fibrinogen<sup>467</sup>, fibrinogen<sup>468</sup>, fibrinogen<sup>469</sup>, fibrinogen<sup>470</sup>, fibrinogen<sup>471</sup>, fibrinogen<sup>472</sup>, fibrinogen<sup>473</sup>, fibrinogen<sup>474</sup>, fibrinogen<sup>475</sup>, fibrinogen<sup>476</sup>, fibrinogen<sup>477</sup>, fibrinogen<sup>478</sup>, fibrinogen<sup>479</sup>, fibrinogen<sup>480</sup>, fibrinogen<sup>481</sup>, fibrinogen<sup>482</sup>, fibrinogen<sup>483</sup>, fibrinogen<sup>484</sup>, fibrinogen<sup>485</sup>, fibrinogen<sup>486</sup>, fibrinogen<sup>487</sup>, fibrinogen<sup>488</sup>, fibrinogen<sup>489</sup>, fibrinogen<sup>490</sup>, fibrinogen<sup>491</sup>, fibrinogen<sup>492</sup>, fibrinogen<sup>493</sup>, fibrinogen<sup>494</sup>, fibrinogen<sup>495</sup>, fibrinogen<sup>496</sup>, fibrinogen<sup>497</sup>, fibrinogen<sup>498</sup>, fibrinogen<sup>499</sup>, fibrinogen<sup>500</sup>, fibrinogen<sup>501</sup>, fibrinogen<sup>502</sup>, fibrinogen<sup>503</sup>, fibrinogen<sup>504</sup>, fibrinogen<sup>505</sup>, fibrinogen<sup>506</sup>, fibrinogen<sup>507</sup>, fibrinogen<sup>508</sup>, fibrinogen<sup>509</sup>, fibrinogen<sup>510</sup>, fibrinogen<sup>511</sup>, fibrinogen<sup>512</sup>, fibrinogen<sup>513</sup>, fibrinogen<sup>514</sup>, fibrinogen<sup>515</sup>, fibrinogen<sup>516</sup>, fibrinogen<sup>517</sup>, fibrinogen<sup>518</sup>, fibrinogen<sup>519</sup>, fibrinogen<sup>520</sup>, fibrinogen<sup>521</sup>, fibrinogen<sup>522</sup>, fibrinogen<sup>523</sup>, fibrinogen<sup>524</sup>, fibrinogen<sup>525</sup>, fibrinogen<sup>526</sup>, fibrinogen<sup>527</sup>, fibrinogen<sup>528</sup>, fibrinogen<sup>529</sup>, fibrinogen<sup>530</sup>, fibrinogen<sup>531</sup>, fibrinogen<sup>532</sup>, fibrinogen<sup>533</sup>, fibrinogen<sup>534</sup>, fibrinogen<sup>535</sup>, fibrinogen<sup>536</sup>, fibrinogen<sup>537</sup>, fibrinogen<sup>538</sup>, fibrinogen<sup>539</sup>, fibrinogen<sup>540</sup>, fibrinogen<sup>541</sup>, fibrinogen<sup>542</sup>, fibrinogen<sup>543</sup>, fibrinogen<sup>544</sup>, fibrinogen<sup>545</sup>, fibrinogen<sup>546</sup>, fibrinogen<sup>547</sup>, fibrinogen<sup>548</sup>, fibrinogen<sup>549</sup>, fibrinogen<sup>550</sup>, fibrinogen<sup>551</sup>, fibrinogen<sup>552</sup>, fibrinogen<sup>553</sup>, fibrinogen<sup>554</sup>, fibrinogen<sup>555</sup>, fibrinogen<sup>556</sup>, fibrinogen<sup>557</sup>, fibrinogen<sup>558</sup>, fibrinogen<sup>559</sup>, fibrinogen<sup>560</sup>, fibrinogen<sup>561</sup>, fibrinogen<sup>562</sup>, fibrinogen<sup>563</sup>, fibrinogen<sup>564</sup>, fibrinogen<sup>565</sup>, fibrinogen<sup>566</sup>, fibrinogen<sup>567</sup>, fibrinogen<sup>568</sup>, fibrinogen<sup>569</sup>, fibrinogen<sup>570</sup>, fibrinogen<sup>571</sup>, fibrinogen<sup>572</sup>, fibrinogen<sup>573</sup>, fibrinogen<sup>574</sup>, fibrinogen<sup>575</sup>, fibrinogen<sup>576</sup>, fibrinogen<sup>577</sup>, fibrinogen<sup>578</sup>, fibrinogen<sup>579</sup>, fibrinogen<sup>580</sup>, fibrinogen<sup>581</sup>, fibrinogen<sup>582</sup>, fibrinogen<sup>583</sup>, fibrinogen<sup>584</sup>, fibrinogen<sup>585</sup>, fibrinogen<sup>586</sup>, fibrinogen<sup>587</sup>, fibrinogen<sup>588</sup>, fibrinogen<sup>589</sup>, fibrinogen<sup>590</sup>, fibrinogen<sup>591</sup>, fibrinogen<sup>592</sup>, fibrinogen<sup>593</sup>, fibrinogen<sup>594</sup>, fibrinogen<sup>595</sup>, fibrinogen<sup>596</sup>, fibrinogen<sup>597</sup>, fibrinogen<sup>598</sup>, fibrinogen<sup>599</sup>, fibrinogen<sup>600</sup>, fibrinogen<sup>601</sup>, fibrinogen<sup>602</sup>, fibrinogen<sup>603</sup>, fibrinogen<sup>604</sup>, fibrinogen<sup>605</sup>, fibrinogen<sup>606</sup>, fibrinogen<sup>607</sup>, fibrinogen<sup>608</sup>, fibrinogen<sup>609</sup>, fibrinogen<sup>610</sup>, fibrinogen<sup>611</sup>, fibrinogen<sup>612</sup>, fibrinogen<sup>613</sup>, fibrinogen<sup>614</sup>, fibrinogen<sup>615</sup>, fibrinogen<sup>616</sup>, fibrinogen<sup>617</sup>, fibrinogen<sup>618</sup>, fibrinogen<sup>619</sup>, fibrinogen<sup>620</sup>, fibrinogen<sup>621</sup>, fibrinogen<sup>622</sup>, fibrinogen<sup>623</sup>, fibrinogen<sup>624</sup>, fibrinogen<sup>625</sup>, fibrinogen<sup>626</sup>, fibrinogen<sup>627</sup>, fibrinogen<sup>628</sup>, fibrinogen<sup>629</sup>, fibrinogen<sup>630</sup>, fibrinogen<sup>631</sup>, fibrinogen<sup>632</sup>, fibrinogen<sup>633</sup>, fibrinogen<sup>634</sup>, fibrinogen<sup>635</sup>, fibrinogen<sup>636</sup>, fibrinogen<sup>637</sup>, fibrinogen<sup>638</sup>, fibrinogen<sup>639</sup>, fibrinogen<sup>640</sup>, fibrinogen<sup>641</sup>, fibrinogen<sup>642</sup>, fibrinogen<sup>643</sup>, fibrinogen<sup>644</sup>, fibrinogen<sup>645</sup>, fibrinogen<sup>646</sup>, fibrinogen<sup>647</sup>, fibrinogen<sup>648</sup>, fibrinogen<sup>649</sup>, fibrinogen<sup>650</sup>, fibrinogen<sup>651</sup>, fibrinogen<sup>652</sup>, fibrinogen<sup>653</sup>, fibrinogen<sup>654</sup>, fibrinogen<sup>655</sup>, fibrinogen<sup>656</sup>, fibrinogen<sup>657</sup>, fibrinogen<sup>658</sup>, fibrinogen<sup>659</sup>, fibrinogen<sup>660</sup>, fibrinogen<sup>661</sup>, fibrinogen<sup>662</sup>, fibrinogen<sup>663</sup>, fibrinogen<sup>664</sup>, fibrinogen<sup>665</sup>, fibrinogen<sup>666</sup>, fibrinogen<sup>667</sup>, fibrinogen<sup>668</sup>, fibrinogen<sup>669</sup>, fibrinogen<sup>670</sup>, fibrinogen<sup>671</sup>, fibrinogen<sup>672</sup>, fibrinogen<sup>673</sup>, fibrinogen<sup>674</sup>, fibrinogen<sup>675</sup>, fibrinogen<sup>676</sup>, fibrinogen<sup>677</sup>, fibrinogen<sup>678</sup>, fibrinogen<sup>679</sup>, fibrinogen<sup>680</sup>, fibrinogen<sup>681</sup>, fibrinogen<sup>682</sup>, fibrinogen<sup>683</sup>, fibrinogen<sup>684</sup>, fibrinogen<sup>685</sup>, fibrinogen<sup>686</sup>, fibrinogen<sup>687</sup>, fibrinogen<sup>688</sup>, fibrinogen<sup>689</sup>, fibrinogen<sup>690</sup>, fibrinogen<sup>691</sup>, fibrinogen<sup>692</sup>, fibrinogen<sup>693</sup>, fibrinogen<sup>694</sup>, fibrinogen<sup>695</sup>, fibrinogen<sup>696</sup>, fibrinogen<sup>697</sup>, fibrinogen<sup>698</sup>, fibrinogen<sup>699</sup>, fibrinogen<sup>700</sup>, fibrinogen<sup>701</sup>, fibrinogen<sup>702</sup>, fibrinogen<sup>703</sup>, fibrinogen<sup>704</sup>, fibrinogen<sup>705</sup>, fibrinogen<sup>706</sup>, fibrinogen<sup>707</sup>, fibrinogen<sup>708</sup>, fibrinogen<sup>709</sup>, fibrinogen<sup>710</sup>, fibrinogen<sup>711</sup>, fibrinogen<sup>712</sup>, fibrinogen<sup>713</sup>, fibrinogen<sup>714</sup>, fibrinogen<sup>715</sup>, fibrinogen<sup>716</sup>, fibrinogen<sup>717</sup>, fibrinogen<sup>718</sup>, fibrinogen<sup>719</sup>, fibrinogen<sup>720</sup>, fibrinogen<sup>721</sup>, fibrinogen<sup>722</sup>, fibrinogen<sup>723</sup>, fibrinogen<sup>724</sup>, fibrinogen<sup>725</sup>, fibrinogen<sup>726</sup>, fibrinogen<sup>727</sup>, fibrinogen<sup>728</sup>, fibrinogen<sup>729</sup>, fibrinogen<sup>730</sup>, fibrinogen<sup>731</sup>, fibrinogen<sup>732</sup>, fibrinogen<sup>733</sup>, fibrinogen<sup>734</sup>, fibrinogen<sup>735</sup>, fibrinogen<sup>736</sup>, fibrinogen<sup>737</sup>, fibrinogen<sup>738</sup>, fibrinogen<sup>739</sup>, fibrinogen<sup>740</sup>, fibrinogen<sup>741</sup>, fibrinogen<sup>742</sup>, fibrinogen<sup>743</sup>, fibrinogen<sup>744</sup>, fibrinogen<sup>745</sup>, fibrinogen<sup>746</sup>, fibrinogen<sup>747</sup>, fibrinogen<sup>748</sup>, fibrinogen<sup>749</sup>, fibrinogen<sup>750</sup>, fibrinogen<sup>751</sup>, fibrinogen<sup>752</sup>, fibrinogen<sup>753</sup>, fibrinogen<sup>754</sup>, fibrinogen<sup>755</sup>, fibrinogen<sup>756</sup>, fibrinogen<sup>757</sup>, fibrinogen<sup>758</sup>, fibrinogen<sup>759</sup>, fibrinogen<sup>760</sup>, fibrinogen<sup>761</sup>, fibrinogen<sup>762</sup>, fibrinogen<sup>763</sup>, fibrinogen<sup>764</sup>, fibrinogen<sup>765</sup>, fibrinogen<sup>766</sup>, fibrinogen<sup>767</sup>, fibrinogen<sup>768</sup>, fibrinogen<sup>769</sup>, fibrinogen<sup>770</sup>, fibrinogen<sup>771</sup>, fibrinogen<sup>772</sup>, fibrinogen<sup>773</sup>, fibrinogen<sup>774</sup>, fibrinogen<sup>775</sup>, fibrinogen<sup>776</sup>, fibrinogen<sup>777</sup>, fibrinogen<sup>778</sup>, fibrinogen<sup>779</sup>, fibrinogen<sup>780</sup>, fibrinogen<sup>781</sup>, fibrinogen<sup>782</sup>, fibrinogen<sup>783</sup>, fibrinogen<sup>784</sup>, fibrinogen<sup>785</sup>, fibrinogen<sup>786</sup>, fibrinogen<sup>787</sup>, fibrinogen<sup>788</sup>, fibrinogen<sup>789</sup>, fibrinogen<sup>790</sup>, fibrinogen<sup>791</sup>, fibrinogen<sup>792</sup>, fibrinogen<sup>793</sup>, fibrinogen<sup>794</sup>, fibrinogen<sup>795</sup>, fibrinogen<sup>796</sup>, fibrinogen<sup>797</sup>, fibrinogen<sup>798</sup>, fibrinogen<sup>799</sup>, fibrinogen<sup>800</sup>, fibrinogen<sup>801</sup>, fibrinogen<sup>802</sup>, fibrinogen<sup>803</sup>, fibrinogen<sup>804</sup>, fibrinogen<sup>8</sup>