

## ONLINE SUPPLEMENT

This repository has been provided by the authors to give readers additional information about their work.

Supplement to: **ADRB2 Gly16Arg polymorphism, asthma control and lung function decline**

By: Cristina Rebordosa, Manolis Kogevinas, Stefano Guerra, Francesc Castro-Giner, Deborah Jarvis, Lucia Cazzoletti, Isabelle Pin, Valerie Siroux, Matthias Wjst, Josep Maria Antò, Roberto de Marco, Xavier Estivill, Angelo G Corsico, Rune Nielsen, and Christer Janson

**Table E1.** Relative risk ratios of partially controlled (grey) and uncontrolled (white) asthma according to ADRB2 Gly16Arg genotypes, and stratified by ICS and LABA use in the last 12 months as reported in the ECRHS II (N=604).

Population and category of risk; partially controlled (pc) and (uc) uncontrolled				Risk of partially controlled and uncontrolled asthma							
				Use of ICS	Use of LABA	per each Arg allele (additive)			among Arg/Arg (vs. Gly/Gly)		
						OR	95%CI	p-value	OR	95%CI	p-value
<i>all asthmatics</i>	pc	-	-	1.37	(1.01 - 1.84)	0.040	1.86	(1.00 - 3.45)	0.050		
	uc	-	-	1.27	(0.92 - 1.76)	0.151	1.53	(0.77 - 3.04)	0.227		
<i>nonusers of ICS</i>	pc	no	-	1.68	(1.14 - 2.49)	<b>0.009</b>	2.45	(1.10 - 5.44)	0.027		
	uc	no	-	1.97	(1.18 - 3.31)	0.010	3.51	(1.04 - 11.87)	0.043		
<i>users of ICS</i>	pc	yes	-	1.07	(0.63 - 1.81)	0.801	1.27	(0.41 - 3.90)	0.675		
	uc	yes	-	0.98	(0.58 - 1.66)	0.943	1.07	(0.34 - 3.32)	0.911		
<i>nonusers of LABA</i>	pc	-	no	1.32	(0.96 - 1.82)	0.089	1.74	(0.89 - 3.42)	0.107		
	uc	-	no	1.40	(0.97 - 2.01)	0.070	1.86	(0.86 - 4.01)	0.117		
<i>users of LABA</i>	pc	-	yes	1.71	(0.70 - 4.20)	0.238	2.38	(0.38 - 14.89)	0.353		
	uc	-	yes	0.96	(0.39 - 2.36)	0.933	0.78	(0.12 - 4.98)	0.796		
<i>nonusers of ICS + nonusers of LABA</i>	pc	no	no	1.52	(1.02 - 2.27)	0.039	2.01	(0.88 - 4.59)	0.099		
	uc	no	no	1.92	(1.12 - 3.29)	0.018	3.05	(0.90 - 10.37)	0.074		
<i>nonusers of ICS + users of LABA</i>	pc	no	yes	na			na				
	uc	no	yes	na			na				
<i>users of ICS + nonusers of LABA</i>	pc	yes	no	1.04	(0.55 - 1.97)	0.902	1.19	(0.29 - 4.86)	0.807		
	uc	yes	no	1.08	(0.57 - 2.05)	0.820	1.22	(0.29 - 5.16)	0.786		
<i>users of ICS + users of LABA</i>	pc	yes	yes	1.22	(0.48 - 3.07)	0.679	1.35	(0.19 - 9.62)	0.764		
	uc	yes	yes	0.81	(0.32 - 2.03)	0.647	0.69	(0.10 - 4.89)	0.710		

\*adjusted for adjusted for sex, age, body mass index and bronchial hyperresponsiveness. Additive models were estimated by modeling the categorical ADRB2 genotype variable as continuous. n.a stands for not available. In bold, p-values that passed Bonferroni correction for multiple testing ( $p < 0.05/18 = 0.0028$ ).

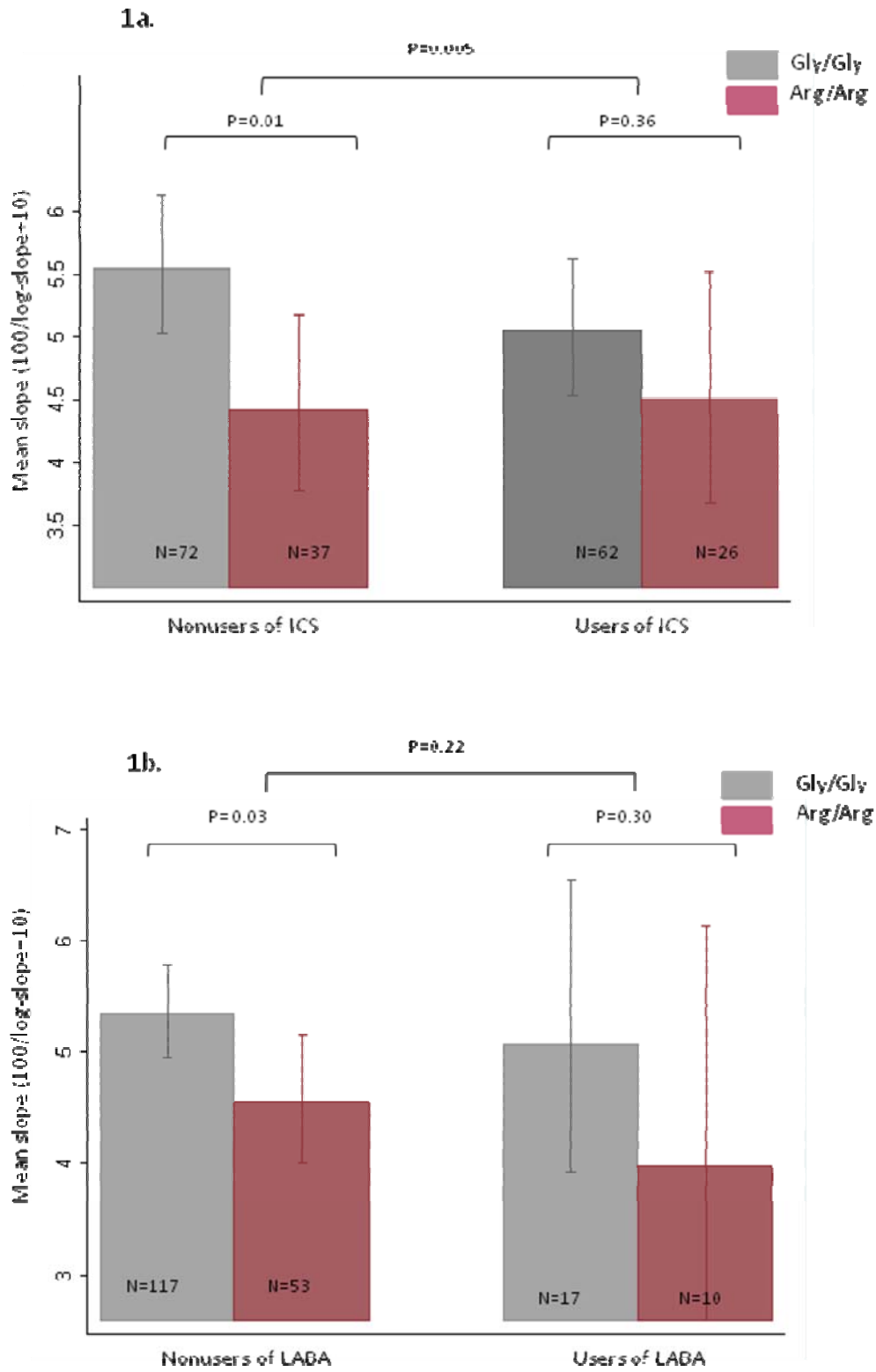
**Table E2.** Odds ratios of Bronchial Hyperresponsiveness according to Gly16Arg genotypes and stratified by ICS and LABA use the last 12months in ECRHS II (N=375).

Population	Use of ICS	Use of LABA	Risk of partially Bronchial Hyperresponsiveness							
			per each Arg allele (additive)				among Arg/Arg (vs. GlyGly)			
			N	OR	95%CI	p-value	N	OR	95%CI	p-value
<i>all asthmatics</i>	-	-	375	1.46	(1.09- 1.96)	0.011	204	2.12	(1.15- 3.89)	0.016
<i>nonusers of ICS</i>	no	-	220	1.53	(1.04- 2.26)	0.031	112	2.51	(1.12- 5.63)	0.025
<i>users of ICS</i>	yes	-	151	1.49	(0.94- 2.38)	0.092	90	1.77	(0.69- 4.57)	0.234
<i>nonusers of LABA</i>	-	no	322	1.44	(1.05- 1.98)	0.022	173	2.12	(1.09- 4.10)	0.026
<i>users of LABA</i>	-	yes	50	1.64	(0.72- 3.77)	0.241	29	2.10	(0.41- 10.66)	0.371

\* Additive models were estimated by modeling the categorical ADRB2 genotype variable as continuous. No p-values passed

Bonferroni correction for multiple testing ( $p < 0.05/6 = 0.0083$ ).

**Figure 1.** Mean dose-response slopes from the methacholine challenge test in Arg/Arg subjects and Gly/Gly subjects stratified by ICS use (**1a**) or LABA use (**1b**).



**Figure 2.** Median dose-response slopes from the methacholine challenge test in users and nonusers of ICS (2a) and in LABA (2b), stratified by Arg/Arg and Gly/Gly genotype.

