International Society for Clinical Biostatistics NEWS

Number 62 December 2016 Editor: David W. Warne

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		Past President, News Editor, Webmaster	David W. Warne (CH)

Website and Email Addresses

www www.iscb.info
Permanent Office office@iscb.info [Rita Schou]

Social Media

LinkedIn http://www.linkedin.com/groups?home=&gid=4795649
Facebook https://www.facebook.com/groups/139123109663/
Twitter @ISCB_Info

ISCB News: Correspondence Address

ISCB News Editor newslettereditor@iscb.info David W. Warne
ISCB Book Review Editor bookrevieweditor@iscb.info Jindra Reissigova

Chairs/Secretaries of Subcommittees (SCs) 2017

Student Conference Awards	Nadine Binder (DE)	Katherine Lee (AU)
Statistics in Regulatory Affairs	Harbajan Chadha-Boreham (FR)	Nicole Close (US)
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Conference Organising	Geir Egil Eide (NO)	Joerg Assmus (NO)

NG Representatives/Deputies/Treasurers/Webmasters/Websites 2017

Czech Rep.	Zdenek Valenta	zdenek.valenta@me.com	sites.google.com/site/iscbcr/home
	Marek Maly	mmaly@szu.cz	
	Jindra Reissigová	reissigova@cs.cas.cz	
Hungary	Julia Singer	jlsngr@gmail.com	efabis.univet.hu:8080/biostat
	Krisztina Boda	boda.krisztina@gmail.com	
	Péter Vargha	varpet51@gmail.com	
Poland	Krystyna Szafraniec	mygomola@cyf-kr.edu.pl	www.iscb.pl
	Alicja Cicha-Mikołajcz	alicja.cichamikolajczyk@gmail.com	
	Kinga Sałapa	kinga.salapa@uj.edu.pl	
Romania	Anca Vitcu	avitcu@yahoo.com	iscbrng.vv.si
	Anca Ignat	ancai@info.uaic.ro	
	Elena Mitocariu	elenamitoca@yahoo.com	

Editorial

After another large conference in Birmingham, ISCB is looking forward to returning to Spain after 22 years for **ISCB38 Vigo 2017**. Judging by progress reports, it will be another large, well-organised event. Jacobo de Una Alvarez and Lupe Gomez of the LOC and SPC have written an article to provide an overview, and more details can be found at www.iscb2017.info. NB it's 6 weeks earlier than normal in 2017, so please plan your holidays accordingly!

A highlight of ISCB37 in Birmingham was the new **Students' Day**, organised by the StCA. This was such a success, the day will be held again at ISCB38.

The **ISCB Election** was held in October-November and you can see the composition of the new ExCom for 2017-18. Congratulations to the winners.

Thanks to the many contributors to this News: Zdenek Valenta and Nadine Binder of the NatG and StCA SCs for information about the 2017 **CASc and StCA awards** to be presented in Vigo, as well as Juan Carlos Pardo-Fernández for **Conference Fund for Developing Countries (CFDC) awards** announcement.

Thanks too to outgoing Secretary Vana Sypsa (**AGM minutes**), and **Book Review Editor** Jindra Reissigova and the numerous **book reviewers**. Yes, there are a lot this time, reflecting Jindra's magnificent work on sorting out the backlog of books, advertising them to the membership and collecting and editing reviews for the News. Finally, thanks to Enrico Chavez for another **cartoon**, and Rita Schou of the **ISCB Office** for keeping everything under control.

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ISCB Membership

New members who have joined ISCB by attending the conference in Birmingham have been added to the membership database on an ongoing basis from April. If you haven't yet logged on to the Members Area of the www.iscb.info website, please have a go; if you need any help, please contact office@iscb.info.

	Date	end	end	Dec	Dec	Dec	Dec	Dec	Dec	Dec	Nov	Nov	Dec	Nov	Nov	Nov	Nov	Nov	Dec	Nov	Dec	Dec	Dec	Dec	Dec	Dec	Jun	Dec				
*=host	Conference	89	92	93	94	95	96	97	98	99	00	01	02	03	04	05	06	07	08	09	10	11	12	13	14	15	16	16	17	18	19	20
	Total	**261**	**596**	**715**	**698**	**725**	**702**	**685**	**729**	**818**	**797**	**837**	**825**	**756**	**758**	**620**	**808**	**800**	**921**	**862**	**880**	**864**	**993**	**1028**	**1084**	**1141**	883	**1032**				
	# Countries	**23**	**32**	**32**	**31**	**33**	**34**	**37**	**37**	**41**	**40**	**45**	**41**	**40**	**38**	**39**	**40**	**41**	**42**	**39**	**42**	**41**	**43**	**42**	**55**	**50**	45	**47**				
1.	UK	50	90	176*	120	144	121	128	169*	135	151	153	141	190*	140	109	133	117	114	124	114	99	130	130	121	144	189*	238*				
2.	Poland [NatGrp]		11	11	24	24	30	21	19	26	34	37	41	41	43	40	49	54	62	66	71	78	82	88	88	86	76	76				*
3.	Germany	30	67	75	84	71	78	72	70	186*	90	87	77	61	57	51	73	48	59	72	61	53	78	113*	107	108	70	73				
4.	Romania [NatGrp]						2			4	1	1	1	19	21	30	28	30	31	36	2	67	58	67	72	77	68	68				
5.	France	30	52	62	50	73	67	52	52	49	53	37	93*	31	41	30	57	41	49	49	119*	48	60	66	70	72	42	59				
6.	Hungary [NatGrp]	1	21	17	18	19	25*	27	29	29	33	34	41	48	42	38*	50	44	43	44	42	48	48	49	52	52	52	52				
7.	Netherlands	14*	30	38	33	36	29	31	39	35	33	38	39	33	87*	35	44	41	39	49	56	38	57	55	55	111	42	48				
8.	USA	18	45	40	39	41	40	79*	66	76	77	89	78	75	57	51	67	62	74	67	64	93	66	63	57	57	37	46				
9.	Czech Rep. [NatGrp]			1	1	1	1	1	1	2	2	1	1	1	1	3	17	36	28	44*	30	30	41	40	43	42	43	43				
10.	Switzerland	14	25	22	80*	33	29	24	25	23	18	23	26	22	23	23	55*	28	26	28	30	15	20	29	37	32	17	26				
11.	Australia	6	9	11	6	9	8	11	9	10	12	8	9	14	8	6	11	11	10	13	18	17	23	31	24	25	21	25		*		
12.	Japan	2	6	7	5	7	4	10	13	20	12	11	10	10	10	17	17	27	20	26	24	22	9	38	30	27	25	24				
13.	Denmark	4	58*	38	31	30	32	26	35	38	39	36	46	41	37	37	40	34	154*	54	60	39	50	39	29	29	20	21				
14.	South Korea					3		1						1				1	6	6	6	5	6	15	22	12	18	20				
15.	Belgium	13	22	27	30	30	32	35	29	25	33	36	33	23	27	24	23	32	33	33	32	24	32	35	21	28	15	20			*	
16.	Canada	6	12	14	14	11	13	15	14	9	9	10	14	16	8	12	12	19	22	18	18	68*	14	17	24	27	18	19				
17.	Austria	4	9	11	13	11	16	13	11	15	18	15	13	16	17	15	14	16	17	15	15	9	10	15	45*	15	16	18				
18.	Norway	13	18	25	22	12	18	10	10	11	10	16	16	12	14	12	13	12	19	21	15	15	70	34	27	24	17	17				
19.	Sweden	23	51	53	54	58	64	51	45	38	44	88*	50	36	34	24	23	19	27	19	18	12	26	13	18	15	11	15				
20.	Turkey		1	1						1				1	2	2	3	4	7	2	3	1		2	5	20	11	13				
21.	Italy	16	33	37	32	32	33	26	33	26	63*	29	25	15	25	15	23	24	20	10	15	8	24	9	16	9	11	13				
22.	Spain	10	12	18	12	46*	23	14	16	12	11	11	8	7	15	5	9	8	5	14	14	4	13	10	17	8	8	11	*			
23.	Slovenia		1	2	3	2	1	1	3	2	1	2	1	2	3	3	4	5	5	4	3	6	4	2	7	9	2	9				
24.	Greece		1	1	1				1	1	3	1	6	1	2	2	3	50*	5	7	7	5	7	11	8	13	8	8				
25.	Thailand		1	1		1	1	2	1	1	2	2	2				3							1	3	5	1	8				
26.	India		1	1	1	1	1	1	1	1	2	1	2	2	3	2	2	3	4	4	3	8	8	6	7	3	5	7				
27.	Taiwan										1	1	1	1	1	1			3	7	4	3	5		2	5	6	6				
28.	South Africa		1	4	1	3	2	2	2	2	2	3	3	3	2	3	3	3	2	5	2	4	4	1	2	5	3	5				
29.	Ireland	1	2	3	4	3	4	4	2	3	2	3		1	1				2				1	3	3		3	5				
30.	Bangladesh																		1							4		4				
31.	Finland	2	7	7	9	9	9	7	5	10	9	18	11	7	11	10	6	8	8	9	8	6	9	11	4	7	3	3				
32.	Russia					1	3	3	3	2	2	1	4	3	2	1	1	1	1					1	2	4	3	3				
33.	Slovakia												1			1	2	2	2	2	1	1	1	3	3	3	3	3				
34.	Bulgaria																						1	2	1	2	3	3				
35.	Sri Lanka																1	1	1								3	3				
36.	Portugal	1	3	5	2	2	2	2	5	5	3	4	3	3	1	1	1	2	6	2	7	2	3	1	10	3	2	3				
37.	Kenya		1	1																1					1	1	1	3				
38.	Iran						1	1					1	1	4	1	3	5	1	2	1	6	3		2	9	2	2				
39.	Israel	1	3	4	4	4	4	3	3	4	10	13	10	7	8	3	4	2	2	1	2	2	3	2	7	5	2	2				
40.	Singapore							3	6	4	5	8	5	7	2	4	6	2	4		1	3	3	5	1	3	2	2				
41.	Pakistan								1	1	1									1						2		2				
42.	New Zealand		1		1		2	1	2	2	2	3	3	3	1	2	2	2	5	2	1	3	1	2	3	7	1	1				
43.	Brazil					2						1							1	1	1	2	2	2	2	2	1	1				
44.	Luxembourg																	1				1	2	1	3	2	1	1				
45.	Colombia							1	1		1			1												1	1	1				
46.	Nigeria																									1	1	1				
47.	Egypt											1										1					1	1				
48.	*Serbia*																				*2*	*13*	*13*	*10*	*11*	*16*						
49.	*China*		*1*	*1*	*2*	*3*	*3*	*3*	*3*	*3*	*3*	*3*	*2*								*2*	*2*		*2*	*3*	*2*						
50.	*Mexico*						*1*	*1*	*1*	*1*	*1*	*1*	*2*	*2*	*2*	*1*	*1*		*1*		*1*				*2*	*2*						
51.	*Estonia*											*2*		*1*		*1*	*1*	*1*			*1*				*3*	*2*						
52.	*Malaysia*					*2*	*1*	*2*	*2*	*1*	*1*	*1*	*1*	*1*	*3*	*3*	*2*	*1*	*1*	*2*	*3*	*2*	*1*			*1*						
53.	*Qatar*																					*1*	*1*		*1*	*1*						
54.	*Vietnam*																				*1*		*1*		*3*							
55.	*Jordan*																								*2*							
56.	*Gambia*												*1*												*2*							
57.	*Venezuela*																						*2*	*1*	*1*							
58.	*Saudi Arabia*											*1*					*1*							*3*	*1*						
59.	*Indonesia*						*1*										*1*			*1*					*1*							
60.	*Croatia*									*1*	*1*		*1*												*1*							
61.	*Kuwait*	*1*										*1*													*1*							
62.	*Cyprus*																								*1*							
63.	*Argentina*											*1*											*1*									
64.	*Algeria*																				*2*											
65.	*Cuba*								*2*	*2*	*2*	*2*	*2*		*2*	*1*		*1*	*1*	*1*												
66.	*United Arab Emirates*															*1*		*1*														
67.	*Chile*																	*1*														
68.	*Malawi*												*1*	*1*	*1*																	
69.	*Lithuania*											*2*																				
70.	*Sudan*											*1*																				
71.	*Ukraine*									*1*		*1*																				
72.	*Philippines*									*1*																						
73.	*Zimbabwe*				*1*																											
74.	*Oman*	*1*																														

ISCB President's Farewell Message

From David W. Warne

So, my 2 years of being ISCB President are almost over… Having been Secretary for 4 years, I was prepared for a lot of hard work, but never imagined being President could be so time-consuming. Being below full power for around 6 months after a big bike crash didn't help (2x broken elbow and 1x broken wrist), it was nice to be able to rely on ISCB's Office, Officers, ExCom, SCs and conference organisers to run things smoothly. I'm looking forward to my semi-retirement, returning to my work as News Editor and Webmaster, with lots of ideas how to improve them.

Anyway, what's been happening? The **Ballot** for choosing the new **Executive Committee and Officers** (Vice-President, Secretary and Treasurer) for 2017-18 took place with help from an external company TricTrac, the ISCB Office and ISCB Ballot Committee, Jeremy Taylor, Giota Touloumi and Catherine Quantin. In the months leading up to the vote, I took the role of Nominations Officer to try to encourage nominations for all positions from as many people as possible.

Having approved the candidature of Krakow, Poland for ISCB41 in 2020, the Society is beginning to look for **Conference Candidates** for **2021** and later. If you and your friends and colleagues would like to organise an ISCB conference, now is the time to explore the initial ideas. A good conference can take 5 years from conception to birth!

This year's conference, **ISCB37 Birmingham**, was very exciting and hectic for the President. So many people to talk to, so little time… I had almost chosen Birmingham as my first university 30 years earlier so it was nice to finally have a chance to see the city and its excellent new facilities.

If you attended the conference in Birmingham, you will have seen many interesting sessions and attended some of the social activities. But perhaps you're not aware the Society is active between conferences, especially its 6 **Subcommittees** (SCs). Have you thought about joining one of them? The following summarises their activities.

The **Student Conference Awards SC** continues to review how it can improve its processes and find new ways to get students involved in ISCB. See the articles below about the special Students' Day which took place in Birmingham, which will be held again in Vigo. It was one of the highlights of ISCB37 for me.

The **Statistics in Regulatory Affairs SC** is planning to launch a Wikipedia website linking to various guidances on biostatistics. They had an abstract accepted for ISCB37 in Birmingham and are submitting a paper to Biometrical Journal.

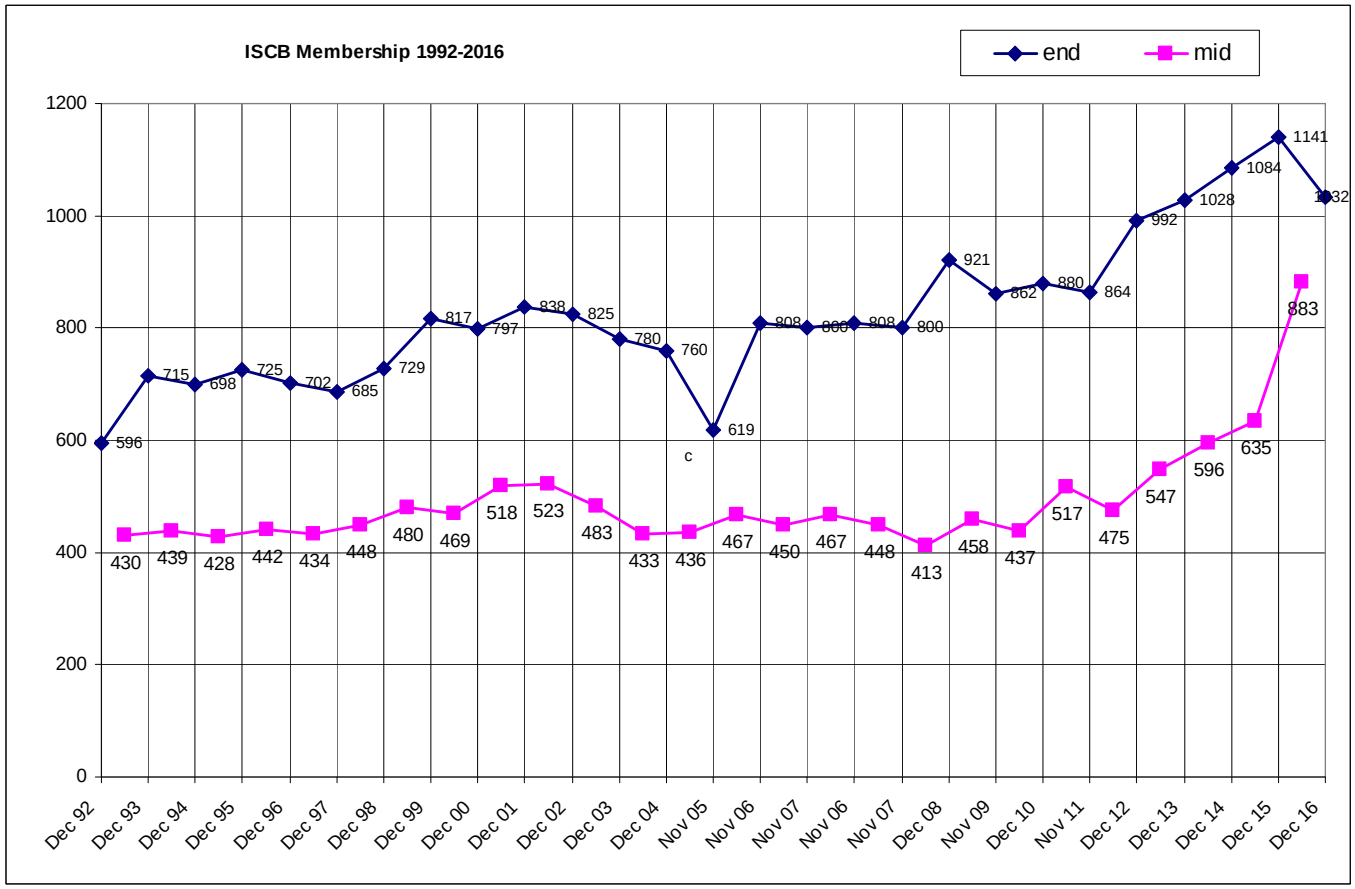
The **National Groups SC** has been very active with the organisation of several seminars within each of the 4 NatG countries. The Terms of Reference have finally been updated and the fees structure updated so that the NatGs make a small contribution to the ISCB income. They will also consider the possibility on setting new National Groups in the future, possibly in countries outside the traditional ones in eastern Europe.

Willi Sauerbrei and members of the **Epidemiology SC** presented updates of the STRATOS initiative in Birmingham, and there's an articles describing STRATOS' past, present and possible future in this News.

The **Education SC** asked for proposals and suggestions for biostatistics courses in 2016 and 2 courses were given in Budapest and Krakow. Proposals for 2017 will be requested in early 2017.

Lastly, the **Conference Organising SC** continues to discuss ways to improve conferences and will advise the Society's Officers on future conference candidates. Guidelines have been sent to potential candidates in 5 countries for 2021+.

ISCB Membership Progression



ISCB Annual General Meeting (AGM) Minutes 2016

From Vana Sypsa, Secretary

Birmingham, Wed 24 August 2016, 12:00-13:00

72 participants: Australia: Katherine Lee, Elaine Pascoe, **Austria**: Michael Schemper, Gerd Rosenkranz, Nicolas Ballarini, Michael Kammer, **Belgium**: Tomasz Burzykowski, **Canada**: Rhonda Rosychuk, Tim Ramsay, **Czech Republic**: Stanislav Katina, Zdenek Valenta, **Denmark**: Niels Keiding, **France**: Harbajan Chadha-Boreham, Joris Giai, Louise Durand, Pascal Roy, Roch Giorgi, Sophie Tezenas du Montcel, Sarah Zohar, **Germany**: Nadine Binder, Andreas Spitzmüller, Ralf Bender, Guenther Kundt, Änne Glass, Lutz Edler, Harald Binder, Irene Schmidtmann, Willi Sauerbrei, **Greece**: Giota Touloumi, Nikos Pantazis, Vana Sypsa, **Hungary**: Julia Singer, **Japan**: Toshiro Tango, **Luxembourg**: Stephen Senn, **Netherlands**: René Eijkemans, Kit Roes, Liesbeth De Wreede, Saskia le Cessie, MarRodríguez-Girondo, **Norway**: Jörg Assmus, **Poland**: Krystyna Szafraniec, Krystyna Stanisz-Wallis, Kinga Salapa, Grazyna Greczka, Milena Balcerzak, **Romania**: Anca Vitcu, **Spain**: Juan Vicente Torres-Martin, Jacobo de Uña-Álvarez, María Xosé Rodríguez-Álvarez, Marta Bofill Roig, Eric Cobo, Nuria Perez-Alvarez, Moises Gomez Mateu, Lupe Gomez, **Sri Lanka**: Roshini Sooriyarachchi, Jayani Chathurangi Hapugoda, A.A. Sunethra, **Switzerland**: Eugenia Migliavacca, David Warne, Diego Kuonen, **UK**: Michael Campbell, Dawn Teare, Marion Procter, Chris Weir, Chris Metcalfe, Jeanine Houwing-Duistermaat, Haiyan Zheng, Lucinda Billingham, Thomas Jaki, Piers Gaunt, **USA**: KyungMann Kim, Nicole Close

President's report - David Warne (DWW)

DWW welcomed the ISCB members attending AGM. He mentioned that since last year there has been a change in the journal where papers presented in the annual conferences are submitted for publication (Biometrical Journal instead of Statistics in Medicine). The Society is progressing over time nicely. The organisers of the conference in Utrecht lowered conference fees and there was still a small surplus. There are approximately 600 participants in Birmingham. DWW reminded that there will be a ballot for ExCom members and Officers this October and invited people interested to join the ExCom to ask for information.

Treasurer's report - Zdenek Valenta (ZV)

According to the treasurer's report, equity and membership are increasing over time. **ZV** presented data on membership by country and type (i.e. regular members, National Groups, Students etc.). He pointed out that the proportion of students is in general rather low, in particular in some countries, and that he would like the Society to adopt more initiatives and funding to attract students.

Concerning the 2017 budget proposal: more money is anticipated from membership fees as compared to 2016 (30,000 instead of 20,000 €). There has been an effort to lower some expenses such as e.g. the cost associated with Officers and ExCom teleconferences. He also announced the changes in membership fees adopted by the ExCom (i.e. 40€ regular fee, 10€ for Developing Countries, 20€ for National Groups). With the proposed budget, the income will be 56,000€ and the expenses 88,000€. This will lead to slight reduction of equity but, as he mentioned, the Society can afford a negative budget. The current equity of 406,000€ is much more than the budget rule (i.e. 3 times the operational expenses, around 150,000 – 180,000€). He reminded that next year, early membership will coincide more or less with early registration for Vigo (as the conference in 2017 will take place in July). Finally, he pointed out that ISCB is doing very well but there are reasons for caution (e.g. volatility in the Euro zone markets, Brexit, refugees, lower expected surplus in future conferences).

Discussion:

KyungMann Kim (KMK) made the comment that the sentence on the impact of European refugee crisis may be difficult to justify as there is no data to support that.

Giota Touloumi made the comment that the Society should rethink the current high conference fees given the very good financial position of ISCB and the difficult situation in many countries. She also proposed that the Society should think how it will be possible to help developing countries and even reconsider what "developing" means. She also mentioned that we could help developing countries through educational courses.

DWW answered that fees are set to balance the budget for a specific number of participants. Each year, the ISCB Treasurer and President discuss with the Local Organisers about the fees. We are close to our aim not to make a lot of surplus. However, we have to be conservative with the budget. We have introduced fees for Developing Countries. Using the World Bank criteria won't solve the issue of some countries that used to be developing are now listed as developed. The Society has also established CFDC for people from developing countries. DWW mentioned that he agrees with ZV that the following years maybe uncertain. The Society welcomes specific proposals. He mentioned that standard forms for these proposals will be created so that they can be discussed in the ExCom. **Giota Touloumi** added that the major problem is the conference registration fees for most people (and not the membership dues to the Society). She also said that EU now considers Greece, Spain and Portugal as low income counties in Horizon 2020 proposals. DWW added that delegates from Developing Countries also benefited from reduced conference fees for the first time.

DWW and **Nicole Close** proposed and seconded the budget proposal for 2017. It was approved unanimously.

Subcommittees' reports for discussion - Motion for continuation

Students Conference Awards: There have been 3 awards this year. Some of the previous award winners are now in the ExCom or presenting at invited sessions or even planning future conferences. Apart from the awards, the Subcommittee (SC) proposes new initiatives for students such as the Students' Day.

Statistics in Regulatory Affairs: They comment on guidelines, circulate them to members and collect their comments. …

National Groups: Apart from activities in the local National groups, the SC is responsible for the Scientists Awards. The Serbian National Group was dissolved as it was not active.

Education: It has been decided by ExCom that the fund for supporting courses will be increased from 3000€ to 5000€ starting from 2017.

Conference Organising: The ExCom approved Krakow's proposal for 2020. This will allow to have lower conference rates in that year to reflect lower costs and to attract biostatisticians from eastern Europe.

Discussion:

KMK asked about STRATOS initiative and whether there is a clearly defined relationship of STRATOS and ISCB. **Willi Sauerbrei** responded that the idea was discussed for the first time in Epidemiology Subcommittee but STRATOS is not part of ISCB. KMK expressed the view that there should be an official documentation about this relationship. **Harbajan Chadha-Boreham** mentioned that the terms of reference of Epidemiology SC include guidelines for epidemiological studies. The SC members recognised the lack of guidelines for observational studies and this is how the idea of STRATOS was formulated. STRATOS has grown and includes members not necessarily from ISCB. She would like to see a bit more discussion in the ExCom on how to maintain links with STRATOS and ISCB.

DWW said that in the Education SC, it has been discussed about expanding the terms of reference and include the support for other educational activates (e.g. webinars). DWW said that in order to vote about this we need a formal proposal to revise the Terms of Reference. It can be reviewed by Officers and the ExCom (we need to check the Constitution). **KMK** thinks it is business of the AGM. **DWW** said not, and after the meeting checked the Constitution which does not say how SCs should be changed, which reminded him that that we may need to have a ballot on changes in the Constitution.

Giota Touloumi made a comment about the fact that there are too many parallel sessions in the conference. **Lucinda Billingham** agreed that ISCB is becoming large and it cannot be organised in the university but rather in an expensive conference site. As a result the conference fees are high and the organisers aim for more participants to be able to cover these expenses. She agrees that this needs re-thinking. **Tomasz Burzykowski** proposed to use Thursday as an additional day (i.e. no mini-symposia).

Giota Touloumi asked how people can join subcommittees. **DWW** answered that they have to ask to join (email members of the SC or ExCom or Officers) and then the members had to be approved.

The continuation of SCs was proposed by **Chris Metcalfe** and seconded by **KMK**. No one was against.

Future conference

Jacobo de Una Alvarez and **Lupe Gomez** presented details about the conference in Vigo 2017.

Elections for the ExCom 2017-18: Results

From Jeremy Taylor, Giota Touloumi, Catherine Quantin, Ballot Committee

A ballot was held for the ISCB Officers and Executive Committee members for the 2017-2018 period. All members of ISCB were eligible to vote. A total of 273 members voted. Congratulations to the following for their election.

For the position of Vice President, **Vana Sypsa** was elected.

For the position of Treasurer, **Zdenek Valenta** was elected.

For the position of Secretary, **Geir Egil Eide** was elected.

For the positions on the Executive Committee the following 8 were elected:

Christopher Weir	**Katherine Lee**	**Stanislav Katina**	**Tomasz Burzykowski**
Hein Putter	**Nadine Binder**	**Thomas Jaki**	**Toshiro Tango**

The STRATOS Initiative - Motivation, Mission, Structure and Main Aims

From Willi Sauerbrei, Michal Abrahamowicz and Saskia Le Cessie, for the STRATOS initiative

According to the general paradigm of modern sciences, statistical methods are key to translate raw empirical data into new insights in, and deeper understanding of, complex processes affecting e.g. human health, the economy, or environment. Yet, the complexity of such processes, and of the observable data they generate, create numerous analytical challenges. In the 21st century, parallel progress in the theory of mathematical statistics and computational resources and technology led to dynamic developments in statistical methodology, resulting in a large number of increasingly complex, ever more flexible, statistical techniques and models that address several complexities frequently encountered in analyzing real-life data. Unfortunately, many of these important developments are ignored in every-day practice of data analysis. Consequently, the design and analysis of recent, often complex and costly, observational studies published in high-impact medical or social sciences journals often exhibit serious weaknesses; frequently resulting in misleading inferences and incorrect conclusions.

Formulating and overcoming these formidable challenges requires a well structured, highly interactive collaboration between a large, international group of statistical experts, whose research combines development of new methodology with collaborative research on real-life applications and whose joint, complementary expertise covers different sub-areas of statistical research. The need for such collaboration arises due to a combination of (i) ever increasing complexity and variety of analytical challenges encountered in observational studies, together with (ii) the increasing trend for narrow specialization, necessary to achieve cutting-edge novel developments in modern statistics. At present, particular challenges are being addressed by leading authorities in different areas of statistical research, but little effort is invested in combining the results of these separate developments and ensuring their material impact on the practice of data analysis. This situation provided the motivation for, and driving vision behind, the STRengthening Analytical Thinking for Observational Studies (STRATOS) initiative.

The ultimate objective of the STRATOS initiative is to develop guidance documents for data analysts and researchers with different levels of statistical training, skills and experience. Specifically, we have identified three levels of statistical knowledge. Initially, we are working to develop guidance documents for experienced statisticians (level 2), which involves drafting reviews of state-of-the-art methods relevant for a number of specific topics (listed below in the table). The guidance documents will cover such practical issues as potential pitfalls due to inappropriate use of 'conventional' methods, the criteria for choice of appropriate, validated methods able to overcome specific challenges, and software to implement these advanced methods. The level 2 guidance results will then be simplified for analysts with low statistical knowledge, including e.g. clinicians and medical students (level 1). In parallel, experts in a specific area (level 3) will help to identify current gaps in knowledge and try to improve, validate and/or compare the existing methods. For more details see Sauerbrei et al (2014) and the STRATOS website http://www.stratos-initiative.org/.

STRATOS as an intellectual child of ISCB

The need to develop guidance for the analysis of observational studies was the first item of the Epidemiology SC (EpidSC) meeting at ISCB2011 in Ottawa. None of the ten present members knew any suitable document and Willi Sauerbrei (WS) proposed that the SC should pursue this challenge. His suggestion was based on very positive experiences in developing reporting guidelines to enhance quality and transparency of health research. During the last two decades reporting guidelines were developed for many types of studies, with the EQUATOR network (http://www.equator-network.org) acting as an umbrella. EpidSC mandated WS to start a project aiming at guidance documents for the analyses of observational data. Several colleagues (most being ISCB members) joined a steering group and the STRATOS initiative was launched with a very successful mini-symposium at the ISCB 2013 meeting in Munich. At each of the ISCB meetings in 2014–16 STRATOS had dedicated invited sessions or mini-symposia (website provides details and slides from all talks). When launching the initiative in August 2013, STRATOS had 45 members. Despite being without official core funding (except use of research funds available to individual members and ISCB support for invited speakers), by November 2016 membership has already increased to more than 80 researchers from 16 countries on 4 continents. This impressive increase reflects the interest of methodologists to work on guidance documents for the analysis of observational studies and the large audiences at all STRATOS sessions and symposia reflect the biostatistical research community's need for such documents.

In July 2016, the STRATOS initiative had its first General Meeting at the Banff International Research Station (BIRS) in the Canadian Rocky Mountains, co-organized by Willi Sauerbrei and Michal Abrahamowicz, and supported by the BIRS grant. During the week-long BIRS workshop entitled 'Developing a Comprehensive, Integrated Framework for Advanced Statistical Analyses of Observational Studies' 38 STRATOS members and 7 research trainees discussed topic-specific and general STRATOS-wide projects (website provides a detailed report). This important meeting informed and stimulated further activities in the following weeks.

Invited, video recorded, STRATOS session at the International Biometric Conference (https://biometricconference.org/), STRATOS Mini-symposium at ISCB2016 http://www.iscb.info/ISCB2016.html), special STRATOS session at the HEC2016 conference (Health—Exploring Complexity: An Interdisciplinary Systems Approach; http://www.hec2016.eu/).

…

Although STRATOS collaborates with several societies and projects, it is a brainchild of ISCB and has closest connections with ISCB and its EpidSC. Many of the ISCB members work with observational data and their numbers are expected to grow as more and more health care data and data from large registries are available for research. The great interest of ISCB members for observational studies and the STRATOS initiative can be seen from the large attendance of the STRATOS sessions at ISCB meetings. Typical ISCB members may be considered experts (level 3) in one or two topics, on which their research focuses, and level 2 analysts in other topics.

The majority of the EpidSC members are also STRATOS members and the majority of the STRATOS steering group members have been active in ISCB, as President, ExCom members, members of SCs and SPCs, presenters of courses and invited speakers.

We expect the ISCB Educ SC (chaired until recently by Catherine Quantin, a STRATOS member) will play an important role in knowledge translation of STRATOS papers and guidance documents, planned for the next year. The STRATOS knowledge translation panel is enthusiastic to help promote activities and encourage adoption of guidance documents among other societies. The overlap in members of EpidSC and STRATOS will ensure that STRATOS documents will be presented at ISCB meetings and educational workshops supported by ISCB; an example is the presentation by WS to the Romanian National Group (see the RNG report 2015, ISCB News # 60).

STRATOS topic groups and cross-cutting panel

STRATOS currently has 9 topic groups (TGs). Topic groups and their chairs are listed in the table. All groups have about 8 to 12 members.

Topic Groups	Chairs
1 Missing data	James Carpenter, Kate Lee
2 Selection of variables and functional forms in multivariable analysis	Michal Abrahamowicz, Aris Perperoglou, Willi Sauerbrei
3 Initial data analysis	Marianne Huebner, Saskia le Cessie, Werner Vach
4 Measurement error and misclassification	Laurence Freedman, Victor Kipnis
5 Study design	Mitchell Gail
6 Evaluating diagnostic tests and prediction models	Gary Collins, Carl Moons, Ewout Steyerberg
7 Causal inference	Els Goetghebeur
8 Survival analysis	Michal Abrahamowicz, Per Kragh Andersen, Terry Therneau
9 High-dimensional data	Lisa McShane, Joerg Rahnenfuehrer

To co-ordinate the activities of different TGs, to share best research practices, and disseminate research tools and results across TGs, several cross-cutting panels have been created recently. These panels aim to address 'generic' issues, such as simulation studies, and publications policies, and to develop recommendations and coordinating the efforts of the individual TGs. Recommendations aim to support, integrate and harmonize work within and across the TGs. They will also help increase transparency in deriving final guidance documents for the entire STRATOS initiative.

The website lists current membership, provides short summaries of topic groups and panels, and includes the link to the detailed report of the BIRS meeting in July 2016.

Recent activities, future challenges and plans

Most STRATOS topic groups will circulate draft guidance documents, focusing on the issues fundamental for their respective areas, by the end of 2018. Some TGs have already derived roadmaps for specific steps and projects necessary to achieve this goal, including validation and comparison of alternative methods in comprehensive, contextually relevant simulation studies.

The emergence of 'Big Data' is a key driver for STRATOS, as this poses particular challenges and opportunities across the spectrum of statistical research and applications. However, the term 'Big Data' encompasses as diverse areas and data sources as electronic health records, large administrative and insurance-oriented databases, related registry data, -omics, and imaging data. Reflecting this diversity, STRATOS deliberately decided not to have a 'Big Data' topic group, but instead to encourage all TGs to consider how their work relates to, can be motivated by, and/or adapted to, specific challenges induced by the type of 'Big Data' relevant to their focus. This process has started in many TGs. The High Dimensional Data TG9 is concerned with the specific analytical problems that arise with -omics data, where the number of variables is typically far greater than the number of study subjects.

We plan to organize a second general STRATOS meeting in 2018, where a key focus will be on novel research projects addressing analytical challenges frequently encountered in real-life observational studies, including the emerging challenges induced by Big Data.

The STRATOS initiative will continue to inform all ISCB members on new insights and guidance documents regarding observational studies.

Sauerbrei W., Abrahamowicz M., Altman D.G., le Cessie S. and Carpenter J. on behalf of the STRATOS initiative. (2014) STRengthening Analytical Thinking for Observational Studies: the STRATOS initiative. Statistics in Medicine, 33: 5413-5432.

http://www.stratos-initiative.org/

From Nadine Binder

Date Thu 25 Aug 2016, 9:00 – 17:00

Aims The Students' Day was intended for ongoing, almost finished or about to start PhD students to:

- Provide a forum for discussing research challenges and experiences on doing good research
- Get advice from invited senior researchers
- Stimulate discussion on how to shape a career in biostatistics

It was initiated by the Student Conference Awards subcommittee (StCA SC) in 2016.

Programme Invited talks were provided by Robin Henderson on "Biostatistical research skills" (9:15-9:45), Katherine Lee on "Developing a Career in Biostatistics" (13:15-13:45), and Hans van Houwelingen on "The Future of Biostatistics" (16:15-16:45).

Students were invited to submit an abstract for an oral presentation (template provided). We primarily aimed for topics reflecting on experiences or questions on doing good biostatistical research, but also allowed for presentations of (preliminary) research results in a less formal environment than the ISCB conference (announced on the conference website as well as through the ISCB mailing list). The submission deadline was shortly after all authors have been notified of their regular conference abstract acceptance. Abstract acceptance notifications for the Students Day were sent out before the Early Bird conference registration closed.

We received 15 well-motivated and fairly diverse submissions from students of different career levels and accepted all of them, resulting in 15 min presentation time for each student (instructions for presentation sent out beforehand).

Four sessions were set up by research content or methods: Session 1 "Challenges in clinical trials" (9:45-10:45), Session 2 "Bayesian techniques" (11:00-12:15), Session 3 "Longitudinal and time-to-event data" (13:45-15:00), and Session 4 "Programming and simulation methods" (15:15-16:15). Each session was chaired by a student and a member of the StCA SC, with the student taking the lead, and was followed by a 15 min discussion slot.

There were three refreshment breaks: morning and afternoon 15 min, and lunch 60 min. The programme and abstracts were included in the main conference book.

Participation Everybody registering as student participant through the conference registration system could check the box for participating in the Students Day. It was free of charge for delegates also attending the main conference, and 30GBP for students attending the day only.

Budget plan A budget plan was set up and approved by the ISCB Treasurer Zdenek Valenta in advance, and we did adhere to the total allocated amount. The room was pre-booked in the conference package, refreshments had a fix per-person price as for the main conference, invited speakers received free entrance to the conference and dinner plus two nights' accommodation. Income was calculated assuming 1/6 Students Day only attendees.

Attendees There were three invited speakers, 14 contributing student speakers (one student cancelled) amongst whom 5 Students' Day only attendees), 59 registered students (53 conference attendees, 6 Students' Day only). Almost 40%, 23 attendees, came from the United Kingdom, 12 from Germany, 5 from The Netherlands, 3 each from Belgium, France, and Italy, 2 each from Denmark and Spain, 1 each from Austria, India, Ireland, Norway, and Slovenia. Guests were President David W. Warne and StCA members, Chris Metcalfe, Hein Putter, and Nadine Binder as session chairs.

Survey At the end of the day, students were asked to complete a feedback form. The form was drafted with help of Tanja Berger, Katherine Lee, Diane Uschner, and Nadine Binder and David W. Warne, and could either be completed in print or online (until 23 Sep 2016). It comprised 19 questions, with answering choices being on a categorical "1-5" scale (Very good, quite good, fair, poor, very poor; Strongly agree, agree, neither agree nor disagree, disagree, strongly disagree), binary ("Yes/No"), with free-text fields, or by choosing from specific question-related text items. We acknowledge the time and effort students spent for completing the questionnaire. We also thank Katherine Lee for transcribing 23 handwritten answers into the online form.

Participants In total, 41 of 59 registered students (69%) answered the questionnaire, and everyone answered all of the 19 questions. The characteristics of responders are as follows: Asking for their current career level, 10% had completed M.Sc., 80% were ongoing PhD students, 8% had recently completed their PhD, and 1 student was an undergraduate. Their current country of residence is: 10 from the United Kingdom, 9 from Germany, 5 from France, 3 from Ireland, 2 each from Belgium, Italy, The Netherlands, and Spain, and 1 each from Austria, Denmark, India, Norway, and Slovenia. Regarding presentation experience, 73% (27%) reported having (not) presented their research at a conference in the past. …

Expectations The responding students reported 1 or more of the following six pre-specified (plus 1 free text) expectations to the day: 73% personal experience of good research; 63% career advice; 56% networking/meet new peers; 32% learning about novel methods, programming tools, or simulation studies; 27% get frank feedback on own research; free text item: "open atmosphere"; "discussing problems in applied methods".

Asking whether the Students' Day met their expectations, 13 (32%) students strongly agreed; 22 (54%) agreed; 5 (12%) neither agreed nor disagreed, and 1 (2%) disagreed. Considering comments, some would have liked more discussions and more networking, and 1 student suggested the latter may be increased by, e.g., "an organised joint lunch".

Invited speakers All responders found the presentations of the invited speakers to be suitably chosen (100% Yes), and an average of 80% rated each single presentation as (very) good in terms of usefulness. Considering individual comments, they specifically liked to learn about the "ups and downs in a research career and the corresponding euphoria and frustration that are accompanied by that", getting motivated "to take part more actively in research, clinical trials and organisation", learning how to handle reviewer comments to own papers, or how to "manage having a family and being successful at work".

Student talks Asked whether the level and content of the student talks met their expectations, 85% of responders (strongly) agreed, and 12% neither agreed or disagreed. Comments said that most of the talks were very good, and only a few fairly abstract talks were hard to follow. Some said they had expected "more focus on the research process and challenges" and that the presentations "should be used to discuss open problems and gain possible solution ideas from the audience and seniors".

Atmosphere We aimed at creating a gentle atmosphere, giving students the chance and enough time for asking questions and allowing for open and constructive discussions. Requesting whether students felt comfortable to ask questions, 37% of respondents strongly agreed; 54% agreed; 7% neither agreed nor disagreed, and 1 student disagreed. Many students (79%) agreed that there was enough time for discussion, while 20% neither agreed nor disagreed. Few commented that "more time would have been better". Correlating with comments on expectations, only 68% students (strongly) agreed that they had enough time for meeting new peers, while 20% neither agreed nor disagreed, and a fairly high amount of 12% disagreed. We further wanted to know whether the Students' Day motivated participants for presenting their own research, and answers were as follows: 39% strongly agreed; 42% agreed; 17% neither agreed nor disagreed; and 1 student strongly disagreed. In comments, 1 student found the day specifically useful "to put myself and my ideas more out there independent of how well my research is progressing".

Overall rating Asking the question: "Overall, how did you like the Students' Day?" response was very positive (61% very good; 34% good; 5% fair). All of the responders would recommend participating in the Students' Day to others (100% Yes).

We further asked participants to describe what they liked most, and amongst they mentioned the good, open and honest atmosphere, the invited talks, talks about the PhD experience and careers, and the discussions as well as the given advice.

Suggestions for improvements We were interested which kind of presentations students would like to see in future Students' Days. Allowing for more than one choice of answer, this is what respondents selected: 85% personal experience; 34% research results; 29% methodology; 29% pharmaceutical industry related; and 24% wished for longer discussion slots. One student explicitly suggested to talk about "how to handle statistical analysis of clinical trials and working with physicians/Common issues in working with real data sets, since it is a large part of our work and can be very frustrating".

"Any other suggestions for improvement" was a free text item and we received fairly detailed and constructive comments. In brief summary, students said we could "possibly add a session/round table on public engagement", have "more discussions about general student life issues: work/life balance, dealing with pitfalls in research, issues with advisors, family planning & career" or "more talks about careers of biostatisticians inside and outside university". It was also suggested to split the day in 2, "giving 1/3 or 1/2 of the course on Sunday and the last part on Thursday".

Next steps We are pleased, the ExCom decided to repeat this initiative during next years' conference in Vigo. In a team of some StCA SC members, a liaison person from the Vigo LOC and some students stating their interest in supporting with organising next years' Students' Day, we will work out and decide on which aspects to keep and which to change in setting up a suitable programme. Specifically, will elaborate on better explaining the day's purpose, explore ways of finding more time for networking and discussions and possibly "integrating" with the students' gathering on Sunday. We will also seek for new senior invited speakers.

National Group Report: Hungary

From Júlia Singer, Krisztina Boda and Péter Vargha

The Hungarian National Group has 52 registered members for 2016. We continued with our regular group meetings with lectures given by members as well as by invited speakers.

On the 12 February 2016, we celebrated the 25th anniversary of the foundation of our national group. For this event we invited also our former members (more than 100 members in total these years).

Two members of our group took part in the ISCB conference in Birmingham, in August 2016, with 1 poster presentations.

Our annual general meeting took place on the 20th of May 2016, where the general and financial report of the representatives was accepted through voting by members. It was also voted an increase of membership fee starting from 2016 (full membership fee will be approx. 10 Euros). Later, at the AGM of the Birmingham conference it turned out that this fee does not fit into the new system defined by the ISCB officers, therefore the discussion on membership fees will have to re-opened, and voting will be repeated in November 2016.

On 14-15 October 2016 we had a short course supported by ISCB entitled Statistical Issues in Drug Development, delivered by Stephen Senn. This was the most successful course in our 25-year history in terms of number of participants (53 attendants from different countries: 46 from Hungary, 3 from Romania, 1 from Poland, 2 from Austria and 1 from Germany).

This year there were no applications for the award called “Young biostatistician of the year”.

National Group Report: Czech Republic

From Zdenek Valenta

The Czech National Group of the ISCB currently has 42 members to be reported as ISCB members. One of its members practising in Germany is registered only locally, but pays her full ISCB dues (40 EUR) to the Copenhagen Office in addition to the local membership fee of 200 CZK.

So far the Group organised four seminars this year, one international ISCB course with Prof. Stephen Senn is going to be organised in Prague on Friday 25th November 2016. As has become a tradition, this will again be a non-sponsored course. Via application through the Education SC the ISCB kindly lent her name to the course which is otherwise a typical scenario for organising an ISCB course in biostatistically developed countries. More about the planned course is given below in the last paragraph.

On 31 March 2016, the Group welcomed Patrícia Martinková from the Dept. of Medical Informatics and Biostatistics of the Institute of Computer Science AS CR in Prague. In her talk entitled `Testing for Moderators of Inter-Rater Reliability in Complex Settings as it Applies to Selection Instruments' she introduced a concept of inter-rater reliability (IRR), commonly assessed by intra-class correlation coefficient, an important statistic for describing an extent to which there is consistency amongst two or more raters in assigned measures. In organizational research, the data structure is often hierarchical and designs deviate substantially from the research ideal of a fully crossed design. Previous research has also shown some evidence of existence of moderators of IRR in selection instruments. However, estimation of IRR in more complex multilevel settings accounting for possible moderators of IRR has not been fully addressed. She used mixed-effect models to estimate IRR for rubrics used to rate teacher applicants to a school district. In this complex multilevel context, she estimated within school and across school IRR and tested hypotheses about possible moderators of IRR, such as applicant type (internal or external). She also enumerated direct effect of IRR on predictive power of the selection instrument and its components, and offered practical applications and policy implications of the methods employed.

Marek Brabec from the Dept. of Non-linear Modelling of the Institute of Computer Science AS CR in Prague gave his talk on 21st April 2016. The title of his talk was `Semi-parametric model of the incidence of asthmatic discomfort incorporating the dependence on the state of air pollution'. Marek has shown the results from a static and also dynamic approach to modelling probability of the incidence of asthmatic discomfort depending on the state of the air pollution, specifically on the concentration levels of several key air pollutants. He used semi-parametric additive model of the GAM class with penalisation motivated from various point of views. He introduced parsimonious sub-model of dynamic component based on certain generalisation of 'distributed lags' kind of model used in econometrics. He further talked about new findings learned from analysing recently wrapped up Czech study.

Next speaker, Stanislav Katina from the Institute of Mathematics and Statistics, Faculty of Natural Sciences at the Masaryk University in Brno, gave his talk on 5th May 2016 on behalf of a group of researchers which further included Ivana Horová, Jiří Zelinka and Iveta Selingerová, the 1st author of the contribution. The presentation was entitled `Modeling risk of orthopaedic implant failure using kernel estimation'. The authors used method of kernel smoothing for modelling unconditional and conditional hazard function. They included estimates using Cox proportional hazard model smoothed by kernel methods as well. Attention was paid to comparing the two approaches. The methods were applied to real data from Slovak Arthroplasty Register on artificial hip joint replacement implemented in all 40 orthopaedic and traumatology departments in the Slovak Republic (coverage of 99.9%) with a maximum duration of follow-up of twelve years between Jan 1 2003 to Dec 31 2014. The set of 46 859 operations with 1005 implant failures was stratified based on type of fixation, diagnosis, and gender. Conditionally on age in years the hazard function was calculated for pre-specified subsets of data and visualised as colour-coded surfaces. These results should lead to an improvement of the quality of care for patients with artificial joint replacement.

The most recent seminar took place on 27th April 2016. The Group welcomed Martin Otava from Nonclinical Statistics and Computing, Janssen Research & Development, Belgium. One typical statistical problem in the pharmaceutical research is the assessment of future experiments, which are part of industrial process, based on standardised criteria. Probability of “success” of such experiment may be calculated on the basis of data gathered during previous stages of production. Since multiple criteria are based on individual observation, a frequent solution involves estimating predictive and tolerance intervals which reflect variability of point estimates of the mean and variance. An alternative approach offers Bayesian analysis and a direct estimation of the distribution of individual values. Here the random effects are easily incorporated, often stemming from different sources of variation, and also an easy interpretation of the main result obtained from the analysis, that is a probability of success of a future experiment.

At this time the Group is busy with preparations for a one-day international ISCB course in Biostatistics entitled `An Introduction to Statistical Issues in Drug Development' which will take place in Prague on 25th November 2016. The course will be taught by Prof. Stephen Senn, Ph.D., who is currently heading the Competence Center for Methodology and Statistics at CRP-Santé in Luxembourg. The course will be based on the Second Edition of Stephen's book `Statistical Issues in Drug Development' published by Wiley in 2008. This will be a second course given in Prague under the auspices of the ISCB, the previous course 'Cross-over Trials' he gave in Prague in 2012. Let me just use the words of Franz Koenig who, when announcing his presentation at the IdEal Webinar Series on 25th Oct 2016, referred to Stephen Senn as 'an ISCB legend'. We are therefore obviously very proud to have the opportunity of welcoming Stephen soon in Prague again.

National Group Report: Romania

From Anca Vitcu

2016 was a year during which the Romanian National Network had a lot of small but important events at members' level, creating valuable opportunities to unveil new emerging research topics and emphasize those activities with a special link and impact to the clusters' academic development, as well as team leading strategies at regional and national levels. A follow-up of these events will be a round table discussion addressed on project, program and portfolio management, planned for the spring of 2017. It will be a 3 part series where well-known experts from healthcare and computer science will be brought together to share their best ideas, strategies and practices on clinical research, public health informatics, consumer health informatics and translational bioinformatics. The event will be organised by the RNG in partnership with the Faculty of Computer Science ("Alexandru Ioan Cuza" University of Iasi).

Very active, the Continuing Professional Development Programme built up by the RNG with the support of the ISCB Education Committee and evolving under the ISCB aegis will carry on the tradition to invite high-qualified national and international experts. The topics to be considered for 2017 emphasize R-programming, machine learning, data and text mining, social network analysis, meta-analysis in medical research. The trainings will be held in Sibiu and Iasi in partnership with the Faculty of Computer Science ("Alexandru Ioan Cuza" University of Iasi) and the Faculty of Medicine (ULBS).

Besides the joint cooperation, the RNG members are as usual involved in individual researches, act as coordinators and members of panel conferences and scientific national and international boards.

More information will be available on: http://iscbrng.vv.si/

National Group Report: Poland

From Krystyna Szafraniec

The Polish National Group of ISCB consists of 80 members as of November 2016. Seven young scientists, including two PhD students joined our group this calendar year.

The members of PNG come from all over the country, so full-day scientific meetings are scheduled twice a year, mostly in Krakow in June and December.

This year, the December 2016 meeting was organized in Warszawa in the Institute of Cardiology. Scientific part consisted of two lectures (*Perception of illness and coping with risk factors in IHD patients* and *Novel SES modelling procedure* and *Evaluation of SES differences in lung function in adults)* given by our members, was followed by the General Meeting of the Polish National Group of ISCB. The General Meeting elected the new board: Krystyna Szafraniec, PhD, chair, Alicja Cicha-Mikołajczyk, PhD, vice chair and Kinga Sałapa, MSc, treasurer.

The next scientific meeting took place again in Warszawa during the Tenth International Seminar on Statistics and Clinical Practice, May 15-18, 2016, organized by International Centre of Biocybernetics of the Polish Academy of Science. The PNG have organized a special session addressed to medical doctors, entitled *Statistical standards in medical research, projects and publications*. The session was chaired by our former leader Ewa Kawalec. Overall eleven lectures and posters were presented by members of PNG during this event.

Other activities :

Proposition to organize the 41st Annual ISCB conference in 2020 in Krakow was prepared, presented, and then accepted by the ExCom during the Annual Conference in Birmingham

Five members of the PNG took part in the Annual ISCB conference in Birmingham. Thanks the ISCB for giving support some of them.

Two-day course on *Causal Inference*, with the financial support of the ISCB, was organized in Krakow, September 22-23, 2016. The course was taught by Stijn Vansteelandt, Ghent University (Belgium). 23 participants (out of 25 registered) took part in the course and then highly appraised it.

Half-day session on *Pitfalls in Medical Statistics* during the 9th Conference on Preventive Cardiology, Krakow, November 18-19, 2016, was co-organized, chaired and presentation were given by the PNG members. It received wide reaction from the scientist who in this or another way apply the methods of biostatistics and need to deepen their knowledge; therefore the audience went much beyond the traditional participant's circle of our scientific meetings. As the idea brought a great success we intend to follow it during the upcoming conference in 2017.

The next scientific meeting is scheduled for January 2017 in Krakow.

The homepage www.iscb.pl (in Polish) introduces our Group to Polish statisticians and others who are interested in application statistics to medical research.

Books for Review by Jindra Reissigová (Book Review Editor)

Important note to potential reviewers:

We regularly receive books from publishers for review in the Newsletter. We are most grateful for these "donations", the reviews of which we regard as a service to you, our members. Regretfully, some individuals, despite repeated reminders, neither return a review, nor the book to ISCB... When requesting a book, please remember that you're making a commitment to the Society to do a little work in return for keeping the book. Please do a little work in return for keeping the book and your name will be published in the News and from 2017, on the ISCB website!

For the format and length, please see recent issues of ISCB News. You can send the review in a variety of formats but plain text email, html, RTF or Word are preferred. The reviews may be edited for clarity (English grammar and spelling, punctuation etc.).

If you find titles that you would like to review, please contact us no later than 9 Jan 2017 at bookrevieweditor@iscb.info. The deadline for submitting a review is 9 Apr 2017.

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Author(s)	Books for review: Title	Publisher	Year	ISBN
Ying Kuen Cheung	Dose Finding by the Continual Reassessment Method	CRC	2011	9781420091519
Wei Zhao, Harry Yang (eds.)	Statistical Methods in Drug Combination Studies	CRC	2014	9781482216745
Shigeyuki Matsui, Marc Buyse, Richard Simon	Design and Analysis of Clinical Trials for Predictive Medicine	CRC	2015	9781466558151
Jixian Wang	Exposure-Response Modeling: Methods and Practical Implementation	CRC	2015	9781466573208
Arul Earnest	Essentials of a Successful Biostatistical Collaboration	CRC	2016	9781482226980
Adetayo Kasim, Ziv Shkedy, Sebastian Kaiser, Sepp Hochreiter, Willem Talloen (eds.)	Applied Biclustering Methods for Big and High-Dimensional Data Using R	CRC	2016	9781482208238
Bryan F.J. Manly, Jorge A. Navarro Alberto	Multivariate Statistical Methods: A Primer, Fourth Edition	CRC	2016	9781498728966
Song S. Qian	Environmental and Ecological Statistics with R, Second Edition	CRC	2016	9781498728720
Harry Yang, Jianchun Zhang, Binbing Yu, Wei Zhao	Statistical Methods for Immunogenicity Assessment	CRD	2015	9781498700344
Berk, Richard A.	Statistical Learning from a Regression Perspective	Springer	2016	9783319440484
Jöreskog, Karl G. Olsson, Ulf H. Y. Wallentin, Fan	Multivariate Analysis with LISREL	Springer	2016	9783319331539

Author(s)	Reviews in this issue: Title	Publisher	Year	ISBN	Reviewer (country)
Daniel Commenges, Helene Jacqmin-Gadda	Dynamical Biostatistical Models	CRC	2015	9781498729673	Per Kragh Andersen (DK)
Ian C. Marschner	Inference Principles for Biostatisticians	CRC	2015	9781482222234	Cono Ariti (UK)
David Collett	Modelling Survival Data in Medical Research (3rd ed.)	CRC	2014	9781439856789	Giulia Barbati (IT)
Gianluca Baio	Bayesian Methods in Health Economics	CRC	2012	9781439895559	Anna Bartkowiak (PL)
Cosmatos,Dennis, Chow, Shein-Chung (eds.)	Translational Medicine: Strategies and Statistical Methods	CRC	2008	9781584888727	Erik Cobo (ES)
Chul Ahn, Moonseoung Heo, Song Zhang	Sample Size Calculations for Clustered and Longitudinal Outcomes in Clinical Research	CRC	2015	9781466556263	Sada Nand Dwivedi (IN)
Alessandro Baldi Antognini, Alessandra Giovagnoli	Adaptive Designs for Sequential Treatment Allocation	CRC	2015	9781466505759	Sada Nand Dwivedi (IN)
Alexander R. de Leon, Keumhee Carrière Chough	Analysis of Mixed Data - Methods and Applications	CRC	2013	9781439884713	Abhik Ghosh (NO)

Amanda L. Golbeck, Ingram Olkin, Yulia R. Gel	Leadership and Women in Statistics	CRC	2015	9781482236446	Marianne Huebner (US)
John P. Klein, Hans C. van Houwelingen, Joseph G. Ibrahim, Thomas H. Scheike	Handbook of Survival analysis	CRC	2014	9781466555662	Jordi Cortés Martínez (ES)
Jialiang Li, Shuangge Ma	Survival Analysis in Medicine and Genetics	CRC	2013	9781439893111	Victor Moreno (ES)
Robert D. Gibbons, Anup Amatya	Statistical Methods for Drug Safety	CRC	2015	9781466561847	Maria de Ridder (NL)
Tie-Hua Ng	Noninferiority Testing in Clinical Trials: Issues and Challenges	CRC	2014	9781466561496	Beth Stuart (UK)
Chul Ahn, Moonseoung Heo, Song Zhang	Sample Size Calculations for Clustered and Longitudinal Outcomes in Clinical Research	CRC	2015	9781466556263	Beth Stuart (UK)
Scott M. Berry, Bradley P. Carlin, J. Jack Lee, Peter Muller	Bayesian Adaptive Methods for Clinical Trials	CRC	2010	9781439825488	Susanne Urach (AT)
Byron Jones, Michael G. Kenward	Design and Analysis of Cross-Over Trials (3rd ed.)	CRC	2014	9781439861424	Stephen Walter (CA)

Author(s)	**Sent recently: Title**	**Publisher**	**Year**	**ISBN**	**Reviewer (country)**
Lawrence Kupper, Brian Neelon, Sean M. O'Brien	Exercises and Solutions in Biostatistical Theory	CRC	2010	9781584887225	Cosmina Bondor (RO)
Mark Chang	Monte Carlo Simulation for the Pharmaceutical Industry	CRC	2011	9781439835920	Michal Jakubczyk (PL)
Stewart Anderson	Biostatistics - A Computing Approach	CRC	2012	9781584888345	Caroline E. Haig (UK)
John Crowley, Antje Hoering (eds.)	Handbook of Statistics in Clinical Oncology (3rd ed.)	CRC	2012	9781439862001	Attila Dávid (HU)
Jen-pei Liu, Shein-Chung Chow, Chin-Fu Hsiao (eds.)	Design and Analysis of Bridging Studies	CRC	2012	9781439846346	David W. Warne (CH)
Robert G. Newcombe	Confidence Intervals for Proportions and Related Measures of Effect Size	CRC	2012	9781439812785	David W. Warne (CH)
Jialiang Li, Shuangge Ma	Survival Analysis in Medicine and Genetics	CRC	2013	9781439893111	Zdeněk Valenta (CZ)
Mark Chang	Adaptive Design Theory and Implementation Using SAS and R (2nd ed.)	CRC	2014	9781482256598	Emma Wang (UK)
Christopher Gandrud	Reproducible Research with R and RStudio	CRC	2014	9781466572843	Caroline E. Haig (UK)
Geskus, Ronald B	Data Analysis with Competing Risks and Intermediate States	CRC	2015	9781466570351	Sophie Tézenas du Montcel(FR)
Iftekhar Khan	Design & Analysis of Clinical Trials for Economic Evaluation & Reimbursement: An Applied Approach Using SAS & STATA	CRC	2015	9781466505476	Oke Gerke(DK)
Andrew B. Lawson, Sudipto Banerjee, Robert P. Haining, Maria Dolores Ugarte (eds.)	Handbook of Spatial Epidemiology	CRC	2015	9781482253016	Paul Eilers (NL)

Sent recently (continued)					
Oleksandr Sverdlov (ed.)	Modern Adaptive Randomized Clinical Trials: Statistical and Practical Aspects	CRC	2015	9781482239881	Alexei Kiselev (RU)
Walter R. Young, Ding-Geng (Din) Chen (eds.)	Clinical Trial Biostatistics and Biopharmaceutical Applications	CRC	2015	9781482212181	Cono Ariti (UK)
Paul D. McNicholas	Mixture Model-Based Classification	CRC	2016	9781482225662	Malgorzata Jurkowska (PL)
Jose Casals, Alfredo Garcia-Hiernaux, Miguel Jerez, Sonia Sotoca, A. Alexandre Trindade	State-Space Methods for Time Series Analysis: Theory, Applications and Software	CRC	2016	9781482219593	Paul Eilers (NL)
Joshua Chen, Hui Quan (eds.)	Multiregional Clinical Trials for Simultaneous Global New Drug Development	CRC	2016	9781498701464	Sada Nand Dwivedi (IN)
Robert Elashoff, Gang li, Ning Li	Joint Modeling of Longitudinal and Time-to-Event Data	CRC	2016	9781439807828	Silvana Romio(IT)
Andrew S. Fullerton, Jun Xu	Ordered Regression Models: Parallel, Partial, and Non-Parallel Alternatives	CRC	2016	9781466569737	Marek Brabec (CZ)
Stephen L. George, Xiaofei Wang, Herbert Pang (eds.)	Cancer Clinical Trials: Current and Controversial Issues in Design and Analysis	CRC	2016	9781498706889	Victor Moreno (ES)
Ardo van den Hout	Multi-State Survival Models for Interval-Censored Data	CRC	2016	9781466568402	Morteza Hajihosseini (IR)
Taylor H. Lewis	Complex Survey Data Analysis with SAS	CRC	2016	9781498776776	Christiana Drake (US)
Brockwell, Peter J. Davis, Richard A.	Introduction to Time Series and Forecasting	Springer	2016	9783319298542	Vito D. Bruno (UK)
Knafl, George J. Ding, Kai	Adaptive Regression for Modeling Nonlinear Relationships	Springer	2016	9783319339467	Sorana D. Bolboaca (RO)

Author(s)	**Sent a long time ago: Title**	**Publisher**	**Year**	**ISBN**	**Reviewer (country)**
J. Edward Jackson	A User's Guide to Principal Components	Wiley	2003	9780471471349	Nicole Close (US)
Mark D. Rothmann, Brian L. Wiens, Ivan S.F. Chan	Design and Analysis of Non-inferiority Trials	CRC	2011	9781584888048	Sebastien Marque (FR)
Mohamed M. Shoukri	Measures of Inter-observer Agreement and Reliability (2nd ed.)	CRC	2010	9781439810804	Elisabeth Svensson (SE)

Publisher	Webpages: *(checked 9 November 2016)*
Cambridge University Press	http://www.cambridge.org/ch/academic/subjects/statistics-probability/
CRC (Taylor and Francis)	https://www.crcpress.com/statistics
Oxford University Press	https://global.oup.com/academic/category/medicine-and-health/medical-statistics-and-methodology
Springer	https://www.springer.com/gp/statistics
Wiley*	http://eu.wiley.com/WileyCDA/Section/id-351216.html

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http://www.iscb.info/Members-Area/Welcome.html which includes the book discount and
http://www.iscb.info/Join-Us/Special-Offer-to-Members---Wiley.html which includes the *Statistics in Medicine* special rate.

Book Review by Abhik Ghosh (NO)

Alexander R. de Leon, Keumhee Carrière Chough	Analysis of Mixed Data - Methods and Applications	CRC	2013	9781439884713

The book under review provides an overview of recent advances in methodologies and applications of multivariate data of mixed types. Now-a-days such mixed data arise frequently in many applied sciences like medicine, health, genetics, toxicology, epidemiology, marketing, economics and many more. Although there were several new researches going on worldwide to solve several important issues and challenges related to mixed data, this is the one book that aims to collect all such important developments within one cover to help all the methodologically oriented as well as the applied researchers dealing with mixed data. The book also presents the up-to-date reference articles and books containing useful methodological development or application of mixed data in its bibliography and the preface. The book contains 13 chapters written by several authors worldwide working in the field of mixed data. The editors, A. R. de Leon and K. C. Chough, have done a great job to combine all of them in a coherent piece providing each chapter a common structure besides making them self-independent with proper background references. Hence, although this compilation is not a text-book to the mixed data analysis, as claimed by the editors, it can serve you "an excellent supplement to the textbooks and monographs" on the methodology and applications with mixed data.

The first chapter of the book is written by editors themselves in order to provide a thorough background overview of the mixed data analysis and walk you through its history and recent developments over last two decades. If you are not already familiar with the notations and terminologies with mixed data analysis, this chapter is a perfect starting that will guide and help you to follow the rest of the book.

Although the rest 12 chapters of the book provide different on-going research topics on methodological issues and applications of mixed data, Editors have arranged them suitably in an order to prepare four broad groups. The first group consisting of 3 chapters (Chapter2-4) presents the analysis of multivariate mixed data, whereas the five chapters in the second group (Chapter 5-9) discuss several approaches of joint analysis of mixed data in the clustered design and longitudinal studies with interesting real data illustrations. The third (Chapter 10-11) and fourth (Chapter 12-13) groups both comprise of two chapters each and present respectively the applications of copula models and Bayesian philosophy in analyzing the mixed data.

At the starting of the first board group, Chapter 2 describes the random forests, formed by several univariate trees for each outcome separately or multivariate trees for all outcomes combined, for predicting mixed outcomes. The authors, A. Dine, D. Larocque and F. Bellavance, have examined the prediction performances of the univariate and multivariate random forests through a simulation study under different scenarios of mixed outcomes, along with three 'ad-hoc' proposals for combining them in one final (weighted) prediction. It has been illustrated that such adaptive combinations of the univariate and multivariate random forests provide reasonably good prediction performances depending on the underlying data-generating schemes. Overall, this chapter is more focused on numerical illustrations through a simulation rather than any general theory and hence the conclusions are only indicative.

Chapter 3 then focuses more on applications in the area of genetics and contains a good review of the possible test statistics for studying the association between the genetic markers (SNPs) and phenotypes (traits) in a genome-wide association study (GWAS). Reviewing the cases of binary or quantitative traits separately, the authors, M. Kwak, G. Zheng and C. O. Wu, have considered the problem of joint association studies for mixed traits of both types with a single genetic marker and illustrated, through appropriate simulations, that such a joint testing can be more powerful than the separate single trait analyses for any genetic marker associated with both types of traits.

Chapter 4 considers the structural equations modelling (SEM) with mixed continuous and discrete data applied widely in social sciences and many other fields. The authors, T. Hoshino and P. M. Bentler, have described several possible approaches of estimation in SEM and the related issues under mixed data. In particular, they have considered the factor score regression methodology in detail and, besides describing its advantages over the classical simultaneous estimation methods, they have also investigated the source of bias in the resulting estimates of parameters associated with the relationship structure of the between latent score variables when the estimated factor scores are used as if they are observed. This chapter provides a very good and detailed theoretical treatment of this important issue in factor score regression and the associated item parcelling methodology (popular in psychology applications) and provides actual expressions for the bias for some existing estimation methods. Here, the authors have also proposed an alternative stepwise estimation method based on the estimated latent factor scores under the mixed continuous, ordinal and nominal data, which is unbiased and consistent in a suitable sense. The theoretical investigations and proposed solution are well-supported by suitable simulation study and real data applications for practitioners.

Motivated through an interesting dataset from medical sciences, namely the Interstitial Cystitis Data Base (ICDB), Chapter 5 considers the problem of joint inference with mixed Poisson (count) and continuous data. The authors, J. Kang and Y. Yang, have reviewed several regression models to analyze such mixed data both with fully parametric and semi-parametric set-ups. They have also discussed two approaches to handle the missing values frequently arising in such biomedical datasets; one of them is based on the classical likelihood approaches with fully parametric set-up. As the second alternative, the authors have proposed a sequential imputation method assuming monotone missing data pattern with missing at random, for the general bivariate longitudinal data set-up of which a special case is the mixed count and longitudinal data. All these methods under complete and missing data set-up are applied to the motivating IC dataset with practical explanations and implications.

Chapter 6 considers the case of mixed binary and continuous data motivated from suitable clinical trial data and presents the comparison and contrast between the multivariate and separate univariate analyses. The authors, A. Teixeira-Pinto and J. Harezlak, have discussed two likelihood-based approaches for joint modelling of such mixed data along with their illustrations and practical implications through application to a motivating dataset. One of these two methods is based on 'top-down' approach of factorization of joint (full) likelihood and fitting model to each of the resulting factorized components. On the contrary, their second proposal is based on 'bottom-up' approach of using latent variable structure to combine and model the correlations between each separate univariate models. Along with a very good description, applications and illustrations of these approaches, authors have also provided the SAS code for their implementation.

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Chapter 7 discusses various approaches of regression modelling for clustered mixed binary and continuous data. Under the assumptions that the observations from the same cluster are exchangeable, the authors, E. O. George, D. Bowman and Q. An, have illustrated a tractable full-likelihood for the fully parametric regression model with mixed binary and continuous outcomes with clustered structure even for large cluster sizes and developed a procedure for obtaining the maximum likelihood estimates of the model parameters. Their main assumption of exchangeability and the inference procedure have been motivated, illustrated and explained through the dose-response modelling of an interesting dataset from developmental toxicity study. Based on joint adverse effects within clusters in such dose-response modelling, the authors have also developed suitable approach for assessing the cluster-specific quantitative risk with their proposed method, whose practical implications are provided with the same real dataset.

Chapter 8 reviews several approaches for joint modelling of longitudinal or clustered mixed discrete and continuous observations that are measured repeatedly in a study. In particular, the author, R. Gueorguieva, focuses on the development and detail descriptions for two particular models to handle such situations with correlated observations, which are the multivariate generalized linear mixed models (M-GLMM) and the correlated Probit models both assuming normally distributed random effects. The first can be applied to data from any combination of distributions but only within the exponential family, whereas the second one may accommodate any general correlation structure but with mixed binary and continuous data. Detailed method of maximum likelihood estimation and related inferences based on these models are described and illustrated through two interesting real data examples. A brief note on the availability of software to perform such analysis is also provided for practitioners.

Likewise in Chapter 8, Chapter 9 also provides some more review of possible approaches generalized linear mixed models for mixed multi-level non-commensurate data. However the main focus of this chapter is on modeling both the correlations between the variables and the correlations due to the repeated measurements or clustering through the multivariate GLMM approach. Considering the increasing computational problem to compute the maximum (full)-likelihood estimates with increasing number of response variables, here the author, C. Faes, has described an alternative “pair-wise pseudo-likelihood” approach. This approach is shown to provide more model flexibility by specifying increasingly complex correlation structures for shared random effects and residual errors, along with feasible computational complexity. One data example from Chapter 8 on the developmental toxicity study has been examined again from these perspectives along with another interesting real life application on a health interview survey.

On the contrary to factorization approach of joint modelling of mixed data discussed in the earlier chapters, Chapter 10 considers the alternative joint-modeling approach of mixed discrete and continuous data by specifying its joint distribution through copulas. The proposed approach is based on the latent variable formulation of mixed data using random effects and hence extends the generalized linear mixed model (GLMM) with normal error and random effects to more general classes with possibly non-normally distributed outcomes. The authors, B. Wu, A. R. de Leon and N. Withanage, formulate the copula modelling of joint discreet and continuous data for independent as well as clustered data cases and discuss the maximum likelihood estimation of the relevant parameters for both the cases. They have also illustrated how the polychoric and polyserial correlations, under two binary or mixed binary-continuous variable pairs respectively, are helpful to incorporate the association between variables in their copula based joint modelling of mixed data. Their proposals are also applied and contrasted to the earlier approaches through the real data example from previous two chapters. However, they have only focused all their analysis based on one particular copula, namely the simplest Gaussian copula, and it works well only for ordinal discrete data mixed with continuous variables. So, as also mentioned by the authors themselves in the end of the chapter, this work needs to be verified for other important copula measures and for the ordinal variables.

Chapter 11 is more application oriented in nature. It reviews and compares both the above approaches, namely the factorization approach of random effect modelling and the copula based joint-modelling approach for mixed discrete and continuous data through application to an interesting econometric dataset from US health economy. Besides illustrating several methodological criticisms of both the approaches, the author, D. M. Zimmer, also provides several interesting economic and health related insights from the data. This chapter is really a good example for any practitioners to understand the applications and interpretations of these methods and to find useful insights from their working dataset.

Chapter 12 focuses on a Bayesian way to address the issue of joint modelling of mixed data through data augmentation. The authors, H. Wagner and R. Tuchler, have considered both the cases of cross-sectional as well as longitudinal data with mixed variable types through a marginal regression models with sparse structure and having (possibly) both fixed or random effects. They have described suitable data augmentation method with latent auxiliary variables and the corresponding modelling of dependence structure among different types of variables via correlated distribution specification. The case of bivariate mixed response having binary and normal components is also described separately. Being a Bayesian procedure, it also involves the relevant descriptions of the prior distributions and the MCMC computational algorithm, which has also been applied to two interesting econometric datasets.

The final chapter, Chapter 13, provides a comprehensive review of available Bayesian methods for modelling the mixed categorical and mixed data. The authors, M. J. Daniels and J. T. Gaskins, describe very clearly the issues and remedies in applications of such Bayesian processes through three interesting real-data examples. Beside others the longitudinal models and modelling dependence there have got slightly more emphasis in the discussions. The issues related to prior selection, in particular the importance of informative priors and the posterior computational issues are reviewed very well. The authors also provide a complete and detailed description of the Bayesian solutions for the issue of incomplete responses in mixed data.

On the whole, the book provides a very useful and descriptive overview of the recent researches and applications in the field of mixed data analysis. The practitioners handling data with mixed discrete and continuous variables will surely get a lot of help and guidance through the discussions and examples presented in the book. Although, most of the chapters of the book is not highly theoretical, the researchers interested in developing the new methods or theories for the mixed data analysis will also get a lot of useful recent ideas in that direction along with suitable references for more detailed theory. Therefore, I think, this book should be a must for any scientist dealing with the problem of analyzing mixed data. And, I would also like to thank the editors, A. R. de Leon and K. C. Chough, for such a nice compilation of very interesting and recent works for us.

Book Review by Marianne Huebner (US)

Amanda L. Golbeck, Ingram Olkin, Yulia R. Gel	Leadership and Women in Statistics	CRC	2015	9781482236446

Various contributors throughout this book answer the question of what leadership is. There is no unique answer to this question as leadership is exercised in a variety of situations, and different skill sets may be needed in different situations.

A statistics leader is defined in the preface as "a statistician who advances the quality of research methods or outcomes, influences others to go down a better path, and makes sure her positive impact on both people and science lasts in her absence."

There is a need for statisticians to exhibit leadership and be proactive due to the expansion of the field of statistics and the gathering of large data sets in all fields. Moreover, since women are making major contributions, the role of women leaders in statistics needs to be explored. Terry Speed in his address as president of the Institute of Mathematical Statistics (IMS) in 2004 pointed out that it is easy to identify "the usual suspects" but it takes conscious and sustained effort to identify and include women. Active recruitment is necessary as "enlightened leadership recognizes that supporting diversity leads to representation, fairness, higher quality of science." (W. Sollecito and L. A. Evarts, Part V).

The book draws upon diverse and rich experiences from leaders in academia, professional societies, and government agencies, but not as much from leaders in industry.

The articles in this book are grouped under the following themes:

Part I: Fundamentals of leadership

Part II: Fresh Opportunities and new challenges for the statistics discipline

Part III: Project leadership

Part IV: Leadership competencies

Part V: Leadership development platforms

Part VI: Individual strategies

Part VII: Institutional and network strategies

It is difficult to do justice to all the important information and recommendations put forth in this book, and much of the material from the book that is not addressed in this review is no less important than what is addressed. So my advice to the reader of this review is: read the book yourself!

Part I discusses important qualities and skills needed for effective leadership and encourages all to step up to leadership roles. Part II points out that robust leadership needs diversity and that women do not advance professionally at the same rate as men. They can be "over mentored" but have insufficient sponsorship. Lynn Billard notes that salary gaps between men and women have widened from 1972 to 2013 and that in the same time period the differentials between the percentage of men and women being tenured were unchanged. Cynthia Clark shares her insights into challenges for program and structural changes in government agencies. Communication is key in project leadership as discussed in part III. Leadership competencies are the focus of part IV. This includes awareness of cultural differences as well as a good understanding of organizational priorities, current trends and policies, and technological advances. It is important, valuable, and necessary to develop leadership skills at all career stages. In Part V a variety of platforms for leadership development are discussed such as professional societies, research teams, and committees. Observing leaders and being aware of their coping mechanisms is a valuable tool throughout anyone's career. Part VI includes contributions about individual strategies that span different types of places. Part VII reinforces the message of the importance of networking. Judith Singer presents six highlights for institutions to foster advancement of women in academe.

There were numerous interesting references throughout this book that I added to my ever-growing reading list. Although some messages are repeated in different articles, they are well worth repeating. Several contributors noted that women obtaining leadership roles depends on others actively facilitating such a process, and that promotion depends heavily on sponsors/champions speaking up for women. A strategy for some women was to develop their leadership potential outside their home institution first. However it is clear that it is up to leaders to create inclusive environments. Life is not equal for male and female statisticians as far as academic positions and work climate are concerned (figures 27.2 and 27.4, Part III).

In summary, this book contains a wealth of information for statisticians considering leadership roles and addresses challenges for women leaders in particular. All contributors are to be complimented on their thoughtful and careful writing about their respective topics. The book is a must read for statisticians in the early stages of their careers, for statisticians looking for leadership advice, for scientists trying to get a better understanding of organizational challenges, and especially for those already serving in leadership positions since leadership is a process requiring continuing education and development. We can learn much from the thoughts and experiences of the contributors.

Book Review by Jordi Cortés Martínez (ES)

John P. Klein, Hans C. van Houwelingen, Joseph G. Ibrahim, Thomas H. Scheike	Handbook of Survival analysis	CRC	2014	9781466555662

This book gives a detailed presentation of modern and advanced techniques for research problems in time-to-event analysis. These are convoluted for various reasons: the presence of censored data, time-dependent covariates and competing-risk, among others. It explains both classical methods and modern techniques without overlooking the Bayesian approach. Its complete overview of the current status of survival analysis should inspire further research in this field.

Several authors share their proficiency on survival analysis, guided by four editors who are also relevant experts on this topic. John P Klein is probably the best known, with books like *Survival Analysis: Techniques for Censored and Truncated Data* (Springer, 2007) and *Survival Analysis: State of the Art* (Kluver, 1992). Klein spent his career as a biostatistician in different research centres such as the University of Missouri, Ohio State University, the Medical College of Wisconsin and the Center for International Blood & Marrow Transplant Research. His long list of publications covers both biostatistical methodology (especially in survival analysis) and cancer research. This was his last book before dying in 2013. Hans C. van Houwelingen is a professor of Biostatistics at Leiden University Medical Center whose main area of interest is medical statistics. He wrote a related book in collaboration with Hein Putter entitled *Dynamic Prediction in Clinical Survival Analysis* (CRC Press, 2011). Joseph G. Ibrahim is currently the principal investigator of two National Institute of Health (NIH) grants for developing statistical methodologies in cancer and genomics research. He is also the Director of the Biostatistics and Data Management Core at UNC's Lineberger Comprehensive Cancer Center. His areas of research focus on missing data, medical imaging analysis, genomics and Bayesian inference. Indeed, one of his most distinguished books is *Bayesian Survival Analysis* (Springer, 2001). Finally, Thomas H. Scheike is a professor in the Department of Biostatistics at the University of Copenhagen. He has written other books on survival analysis, such as *Dynamic Regression Models for Survival Data* (Springer, 2006).

A common feature of books with contributions from various researchers is that some concepts are repeated throughout the book. This can be seen as a drawback, but also as a great advantage, as the reader may have different approaches to the same problem. This is the case here, as nearly every chapter complements the theoretical explanations with examples based on real data (most of them in the medical field) to facilitate understanding, in some cases even providing the analysis codes for different statistical software, mainly R but also SAS and STATA.

There are six main sections: (1) Regression Models for Right Censoring; (2) Competing Risks; (3) Model Selection and Validation; (4) Other Censoring Schemes; (5) Multivariate/Multistate Models; and (6) Clinical Trials. Each of these sections includes several chapters written by one or more reputable authors. The following paragraphs explain each of these sections in depth.

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In the first section, the authors propose various alternatives for analyzing classic survival models with right censoring. The first chapter gives a quick overview of the basic concepts related to survival and hazard functions as well as the formulation of the Cox model and the interpretation of Martingale and Schoenfeld residuals. It is noteworthy that, in most published studies, it is not mentioned whether the Cox model assumptions have been validated. Other more complex problems (solved later in the book) are introduced, such as the presence of left-truncated data and time-dependent covariates. The second chapter deals with the survival problem from a Bayesian perspective, using both fully parametric and semi-parametric models. An interesting explanation for using a piecewise constant hazard function to maintain the premise of a proportional hazard is initially presented and recurs throughout the book. In addition, it illustrates how to take advantage of the data from previous studies to build this piecewise hazard function. Chapters 3 and 4 set forth alternatives to the classic Cox model. Classic variants are described first, such as additive hazard models and semi-parametric and parametric models for accelerated life models. The most interesting part of the fourth chapter is its brief presentation of currently fashionable joint models. The fifth chapter addresses a common issue for all regression models: variable selection. The proposed methods are very close to those that would be used in a linear model: univariate models as a first filter; automatic selection methods for multivariate models; and the possibility of inserting a penalizing function into the partial likelihood function for reducing the number of covariates. Another mentioned alternative is regression analysis with variables resulting from Principal Component Analysis (PCA), which involves results that are less interpretable but more synthetic. This chapter also highlights the importance of having two data sets (training and test) in order to validate the models. The sixth chapter focuses on those models, which are called cure models and are based on the fairly unnecessary premise that the event should appear in the individual later or earlier. The section ends with a masterful explanation of how to relate the causal diagrams within the scope of survival analysis for interpreting the covariates in an etiological way.

The second section addresses competing risks arising when the event of interest may occur for various reasons, but the researcher is interested only in one of these reasons. The eighth chapter presents some general concepts like multistate models (and their advantages over the failure of latent ones) and nonparametric approaches. As in the first section, the next chapter focuses on a Bayesian approach by discussing and emphasizing the interrelationships of three types of models: cause-specific hazards, mixture and sub-distribution models. To help choose from among models, it defines the two most common indicators: DIC (Deviance Information Criteria) and LPML (Pseudo-marginal Likelihood). Chapter 10 explains how to handle pseudo-observations obtained from Jack-knife estimators and use them as outcomes in Generalized Estimating Equations models. This chapter stresses the importance of not only

considering survival times but also the quality of life during the study period by using multistate models to consider the patient's different health states. Chapter 11 presents binomial models in which different time horizons are defined for the outcome, with a logistic regression applied in each one to establish the presence or absence of the event of interest. The section ends with a chapter devoted to comparing different models applied to the same data in a bone marrow transplant study, comparing conventional models with those that take into account competing risks.

The third section focuses on variable selection and the robustness of the Cox model under different scenarios. Regarding the former, Chapter 13 explains the classical criteria for variable selection, doing so similarly to Chapter 5 but by placing more emphasis on the kind of indicator chosen for this process. It highlights the importance of model parsimony and, consequently, recommendations to use measures such as Akaike Information Criteria (AIC) or Bayesian Information Criteria (BIC), which take into account or even introduce penalties into the likelihood function in order to reduce dimensionality. When the target is more predictive than etiologic, the c-statistic is proposed as a measure of interest. One innovative aspect is the division of the study sample into 3 subsamples for selecting candidate variables by cross-validation when constructing the model: two conventional ones (training and validation) and an initial subsample (which may be the same as the training one). Overall, this chapter is undoubtedly one of the most practical because it provides multiple systems to avoid over-fitting, with several examples in both real and simulated data. However, there appears to be a misprint concerning the sizes of the models, making Tables 13.1 and 13.2 inconsistent. The next chapter introduces the concept of the Bayes factor for model selection. In this case, the choice affects several components: covariates to include; a priori assumed distributions; and their hyper-parameters. The recommendation when priors are defined is to use the Bayes factor, whereas if you want to skip this assumption, indicators such as the BIC or the Deviance Information Criteria (DIC) are proposed. Again, measures of the model's predictive ability that are obtained through cross-validation are mentioned. However, an example of application is missing in this chapter. Genetic studies have become increasingly important lately and, along these lines, Chapter 15 addresses the issue of variable selection when its number far exceeds the number of individuals. Two major methods are proposed: firstly, to incorporate penalty functions into the likelihood function in order to reduce the number of covariates (similar to Chapter 13); in addition, they recommend using univariate models to control the multiplicity of the family-wise error rate or the false discovery rate. It is interesting to note that confidence intervals can be obtained for the error estimates in order to know the uncertainty. This section ends with a fairly transversal theme concerning the robustness of the Cox model. In fact, Chapter 16 could have fit in any other section without any problems. The main conclusion is that the partial likelihood estimator is not robust to greatly independent censorship. Authors present another estimator (average regression effect), which is not affected by an increasing proportion of censored data. Moreover, one should take notice of the closely related covariates that arise in observational studies, since classical Cox model analysis leads to severe biases when there is no constant hazard ratio. This topic is not a minor issue, because the Cox model is often chosen out of tradition and not based on statistical criteria.

The fourth section deals with censure structures other than the usual right censoring. Chapter 17 concerns nested case-control and case-cohort designs. This part really could have been included in any book on epidemiology, even outside the scope of survival analysis. It carries out a deep exploration of case-control studies and provides a relevant comparison between estimators and designs, thus showing their strengths and weaknesses. Chapter 18 deals with the interval-censored data produced by some uncertainty about when the event actually occurs. It is an extremely complete chapter, going so far as to even combine competitive and interval-censored problems while providing different functions in SPLUS, SAS and R for this type of analysis. The last chapter explains a particular sort of data that is called current status data, which refers to the situation in which the outcome for each patient is assessed at a specific time and all that is observed is whether he or she has experienced the event before this time, with the relevant analysis being applied to specific data.

The fifth section shows how to analyse and interpret multistate models in which the patient can remain at different levels of health. In these models, both transition intensities (between states) and the marginal rate of the event's occurrence are relevant. Chapter 20 introduces the classical multistate models for addressing these two issues. Chapter 21 provides an alternative to correcting the immortality bias by setting in advance a landmark time point that is deemed large enough to observe a specific treatment effect. The next three chapters (22-24) focus on the problems of dependence that may exist in the multistate models as well as the methodologies to be used (classical, Bayesian or copulas); while the last three chapters (25-27) apply these methods to specific problems in survival analysis.

Finally, the last section focuses on three specific aspects in clinical trials: the calculation of sample size, trials with a sequential design and trials with paired data. Sample size calculation is particularly sensitive in these studies, as it depends on the number of events rather than the number of patients recruited. In Chapter 28, authors propose several methodologies for sample size calculations, from the simplest based on assuming a constant hazard over time to more complex structures based on parametric models that assume varying risks over time. The next chapter treats the subject of sequential design, which is already complex in itself but becomes even more so depending on the sort of endpoint characteristic in survival studies. The author takes the theory that is already known for this type of design and adapts it to this type of study. The last chapter of the book explains the designs in which data is matched by some factor that makes them more similar to each other (i.e. pairs of body parts such as eyes, kidneys or knees, and sibling or twin pairs).

In summary, this book could be useful for graduate students who want to delve into the intricacies of survival analysis, for researchers who want to apply the most advanced methods and for teachers who would like to prepare courses related to this topic. I strongly recommend this book as an important source for going deeper into the analysis of time-to-event data. However, for those who want to make a first approach to this topic, I believe that there are more suitable introductory books for this purpose, for example, *Survival Analysis: A Self-Learning Text (Springer, 2012)*.

Medical and Pharmaceutical **Statistics Research Unit**

Lancaster University

The MPS Research Unit is pleased to announce our programme of short courses for 2017 on advanced concepts in the design and analysis of clinical trials. Our courses are aimed at statisticians working in clinical research. Courses take place in the attractive accommodation of the Postgraduate Statistics Centre at Lancaster University. Presenters will be Thomas Jaki, Philip Pallmann, Andrew Titman and Fang Wan.

CALENDAR FOR 2017

13 Feb - 16 Feb	Pharmacological Modelling
27 Feb - 2 Mar	Survival and Event History Analysis
13 Mar - 16 Mar	Adaptive Methods in Clinical Research
12 June -13 June	Designing Early Phase Trials

FURTHER DETAILS AND BOOKING:
For details of these and other courses offered by the Postgraduate Statistics Centre, go to http://www.lancaster.ac.uk/maths/postgraduate/short-courses-and-cpd/ or contact
Angela Mercer, Postgraduate Statistics Centre, Department of Mathematics and Statistics,
Fylde College, Lancaster University, Lancaster LA1 4YF, UK.
Tel: +44 1524 593064, email: a.j.mercer@lancaster.ac.uk

Cartoon Corner

From Enrico Chavez

ISCB38 Vigo 2017: Conference Awards for Scientists

From Zdenek Valenta

As in previous years, the 2017 ISCB Conference Awards for Scientists (CASc) are available to biostatisticians from countries underdeveloped in clinical biostatistics to attend the 2017 ISCB Annual Conference in Vigo, Spain, and to present a paper there. The CASc budget for 2017 allows for granting at least 3 CASc awards. Please, note that previously awarded applicants are no longer eligible to apply for the CASc award.

Only original contributions, not previously presented or published before the time of application will be considered. Applications with purely theoretical content or those representing mere routine analyses of data sets are not encouraged by ISCB.

Each CASc award will consist of a free *registration* to the 2017 ISCB Annual Conference, free *accommodation*, free subscription to one *short course* selected by the applicant, an invitation to the *Conference Dinner* sponsored by the ISCB, plus a *travel support.*

Scientists should submit their completed application form, one-page abstract and full poster or paper/presentation to Zdeněk Valenta (see the address below).

Abstracts not granted a CASc award will be eligible for independent review by the Vigo Scientific Programme Committee (SPC). However, please note that the abstracts will be forwarded to the SPC only *at the specific request of the applicant.*

Students are not eligible to apply for the ISCB CASc awards. Instead, they are encouraged to apply for the Student Conference Award (ISCB StCA).

Zdeněk Valenta
ISCB National Groups Sub-committee
Dept. of Medical Informatics & Biostatistics
Institute of Computer Science AS CR
Pod Vodárenskou věží 2
182 07 Prague
Czech Republic
Tel: +420 266 052 094
Fax: +420 286 581 453
E-mail: zdenek.valenta@fulbrightmail.org

Full details on the application procedure are given in the full announcement.

Closing date for the applications is **Mon 20 Feb 2017**.

ISCB38 Vigo 2017: Student Conference Awards

From Nadine Binder

The Student Conference Awards are available for registered postgraduate students to attend and present a paper at the 38th ISCB Annual Conference, 9 - 13 July 2017, Vigo, Spain.

Approximately three awards will be granted depending on the number and quality of the applications. Selection will be made on the basis of a summary of a paper to be presented, which should illustrate the application of statistical methodology to clinical or epidemiological research. Results of particular studies are of interest only if the analysis has methodological implications or shows a novel and interesting application of biostatistics.

Applications, prepared as described in this **document**, should be sent by email to the Chair, Nadine Binder, copying the Secretary, Katherine Lee. All applications will be acknowledged, so please look out for an email.

NB Previous winners are not eligible to apply.

Chair: Nadine Binder
Institute for Medical Biometry and Statistics
Medical Center – University of Freiburg
Stefan-Meier-Str. 26
79104 Freiburg
Germany
Tel: +49 761 2036662
Fax: +49 761 2036680
Email: nadine.binder@imbi.uni-freiburg.de

Secretary: Katherine Lee
Email: katherine.lee@mcri.edu.au

The closing date for application is Mon 20 Feb 2017.

ISCB38 Vigo 2017: Students' Day

From Nadine Binder

We welcome all students to join the **Students' Day** during next year's conference in Vigo on Thursday 13 July 2017. The aim of the day is to stimulate discussion on how to be a good researcher and how to come up with biostatistical research projects of ongoing or future interest. We like to share personal experiences about doing biostatistical research and thereby may talk about how to deal with potential pitfalls arising in the research process.

Whether you are just about to start with your PhD studies or will hand in your thesis soon, you may like to meet your peers and exchange your thoughts and ideas, or get to know more about how to shape a career in biostatistics. So, as such, the day complements the regular ISCB conference. For a detailed summary about last years' Students Day, please have a look into the report within this Newsletter.

Programme:

We will have three invited senior speakers who are going to give career advice on strategies for success in biostatistical research, and who will be there to discuss your research challenges with you. The main part of the programme, however, will be composed of your contributions, still allowing sufficient time for discussions. Therefore, we invite you to contribute to the day by submitting an abstract.

Abstract submission

All students, i.e. (to be) graduated within or shortly before 2017 or registered PhD students in 2017 or about to finish doctorate in 2017, are invited to submit an abstract for an oral presentation related to the topics outlined above. The abstract submission deadline is 10 April 2017 (shortly after all authors have been notified of their regular conference abstract acceptance). Abstract acceptance notifications for the Students' Day will be sent out by 25 April 2017 (before Early Bird conference registration closes on Sunday 30 April 2017). You will find more detailed guidelines for abstract submissions on the conference website www.iscb2017.info soon.

Registration

You can register for the Students' Day through the main ISCB conference registration website www.iscb2017.info. Participation will be free of charge for delegates also attending the main conference, and will be 30 EUR for students attending the day only.

ISCB38 Vigo 2017: Conf. Fund for Developing Countries (CFDC)

From Juan Carlos Pardo-Fernández

Financial support to participate in the 38th Annual Conference of the International Society for Clinical Biostatistics (ISCB38) to be held in Vigo, Galicia, Spain from 9-13 July 2017 is available to scientists and students from developing countries (Low, Lower-middle and Upper-middle income economies, as defined according to the World Bank list as of 1 January 2017). In order to qualify, applicants have to submit an abstract for either oral or poster presentation and be selected by the Scientific Programme Committee (SPC) for presentation at ISCB38. Applicants should indicate their request for consideration for the CFDC financial support at the time of abstract submission along with a letter of application (on the official letterhead of the institution where the applicant is enrolled/employed) addressed to:

Juan Carlos Pardo-Fernández
Facultad de Ciencias Económicas y Empresariales
Campus Lagoas-Marcosende, Universidad de Vigo
36310 Vigo
Spain
Tel: +34 986813505
Fax: +34 986812401
Email: juancp@uvigo.es

The closing date for application is the abstract submission closing date of Monday, 20 February 2017, and the applicants will be informed by the CFDC Subcommittee in April 2016 well before the Early Bird registration date of Sunday, 30 April 2017.

The evaluation and selection for the CFDC will be based on the SPC's determination regarding the abstracts for oral/poster presentation. This will be administered by the CFDC Subcommittee comprising Vana Sypsa (ISCB Vice President) as Chair, Juan Carlos Pardo-Fernández (ISCB38 LOC representative), and David Warne (ISCB Past President). Conference registration fees will be waived for those selected for CFDC, and the funds can be used to defray the cost of travel and accommodation, but can only be claimed after attendance and presentation at ISCB38.

The CFDC will be entirely separate from the Conference Award for Scientists (CASc) administered by the National Group Subcommittee and from the Student Conference Awards (StCA) administered by the Student Conference Awards Subcommittee. Those who apply for CASc or StCA, but not selected will automatically be considered for CFDC support if they qualify and will be informed accordingly.

NB Previous winners are not eligible to apply.

From Jacobo de Uña Álvarez (LOC Chair) and Guadalupe Gómez Melis (SPC Chair)

In 2017, the city of Vigo will be hosting the 38th Annual Conference of the ISCB. Vigo is the largest city in Galicia, the autonomous historical region in the NW of Spain. It is surrounded by splendid beaches and mountains, and enjoys a modern, industrial and innovative atmosphere.

Vigo is fully committed to science through the University of Vigo and its faculties and research institutes, like the Biomedical Research Center (CINBIO), launched in 2009 to promote the collaboration with local hospitals and biomedical industry.

About the conference

Like previous annual conferences of ISCB, the 2017 conference will provide an international scientific forum for exchange of theory, methods and applications of biostatistics in medical research. The conference is addressed to statisticians, clinicians and members of other disciplines related to clinical practice, such as epidemiologists, clinical chemists and clinical pharmacologists.

This year, two exciting plenary talks given by Anastasios Tsiatis and Francesca Dominici and eight invited sessions on a number of key topics are organized. This will be completed with contributed parallel sessions about scientific topics of special interest. Besides, several courses and mini-symposia are scheduled, including the Student's Day on Thursday, which follows the successful first experience at ISCB37. We don't forget the traditional excursions on Tuesday and the social events to enjoy Vigo and its surroundings.

The venue

The venue of the conference is the *Mar de Vigo Convention Centre and Auditorium*, an impressive beachfront building designed by the Galician architect César Portela and opened in 2011. Located at a walking distance from some of the best hotels and restaurants in the city centre, *Mar de Vigo* raises at a privileged place between the façade of the fishing port of Vigo and the dockyards, with amazing views of Vigo's estuary (*Ría de Vigo*). The building covers more than 23,000 m2 and holds an auditorium with capacity for about 1,500 people.

We are looking forward to seeing you at the ISCB38 in Vigo. We are sure that the conference will be a great experience!

Plenary sessions (Monday and Wednesday)

Anastasios Tsiatis (Monday). Gertrude M. Cox Distinguished Professor of Statistics from the Department of Statistics at the North Carolina State University (USA). His research focuses on a variety of problems in Biostatistics. This includes developing statistical methods for the design and analysis of clinical trials, censored survival analysis, group sequential methods, inference on Quality Adjusted Lifetime, surrogate markers, semi-parametric methods with missing and censored data, causal inference and dynamic treatment regimes.

Francesca Dominici (Wednesday). Professor of Biostatistics, Senior Associate Dean for Research, and Associate Dean of Information Technology at the Harvard T.H. Chan School of Public Health (USA). Her research focuses on the development of statistical methods for the analysis of large and complex data. She leads several interdisciplinary groups of scientists with the ultimate goal of addressing important questions in environmental health science, climate change, comparative effectiveness research, and health policy.

Pre-conference courses (Sunday)

- Statistical Methods for Microbiome Studies –M. Luz Calle
- Use and Understanding of Causal Methods in Clinical Research – Els Goetghebeur
- Recurrent Event Data Analysis in Clinical Trials –Mouna Akacha, Richard Cook
- Age Period Cohort Models: Frequentist and Bayesian Perspectives –Jon Wakefield
- Advances in Adaptive Clinical Trial Design: Bayesian and Frequentist Approaches –Yannis Jemiai, Pantelis Vlachos

Mini-symposia (Thursday)

- Choosing Estimands in a Clinical Trial –Promoters: Rosa Lamarca, Frank Bretz
- Modelling Personalised Screening: a Step Forward on Risk Assessment Methods –Promoter: Montse Rue
- Statistical Methods for Medical Imaging and their Use in Clinical and Epidemiological Studies –Promoter: María Durban
- Students' Day

Invited sessions (Monday – Wednesday)

- Bayesian Methods in Clinical Research
- Beyond Proportional Hazards
- Biostatistics for High Dimensional Data
- Complex Survival Data
- Joint Modelling in Practice
- Statistical Methods for Precision Medicine
- Clinical Trial Simulations: the When, Where, and What
- Methods in Research on Research

Contributed talks and posters (Monday – Wednesday)

The Scientific Programme Committee particularly encourages submissions of contributed presentations about the aforementioned invited session topics, as well as on further scientific topics of interest, namely:

- STRengthening Analytical Thinking for Observational Studies (STRATOS)
- Statistical Methods in Epidemiology
- Statistical Methods for Systematic Reviews
- Statistical Challenges of EHR (eHealth Records) Analysis
- Pharmaco-epidemiology and Drug Development
- Nonparametric Methods and Goodness-of-Fit in Clinical Research
- Multistate Survival Analysis and Dynamic Prediction
- Multiple Comparison Procedures in Clinical Research
- Multi-regional Clinical Trials
- Machine Learning for Clinical Data Analysis
- Design and Analysis of Vaccine Studies
- Design and Analysis of Clinical Trials

Excursions (Tuesday afternoon)

The Local Organising Committee is offering the most enjoyable excursions to relish Vigo and its surroundings:

- Cíes Islands - Atlantic Islands National Park
- Santiago de Compostela and its Cathedral
- Vigo – Baiona - O Rosal (*Albariño* Wine Valley)
- Vigo Walking City Tour
- River *Miño* Cycling Trail

Social events (Sunday, Monday and Wednesday)

- Student Gathering on Sunday evening
- Welcome Reception on Monday evening
- Conference Dinner on Wednesday evening

Important dates

- Call for abstracts: 20 December 2016
- Deadline abstracts submission: 20 February 2017
- Notification abstracts acceptance: 1 April 2017
- Early bird registration deadline: 30 April 2017

More information

- Please visit our website: www.iscb2017.info
- Email: iscb2017@orzancongres.com

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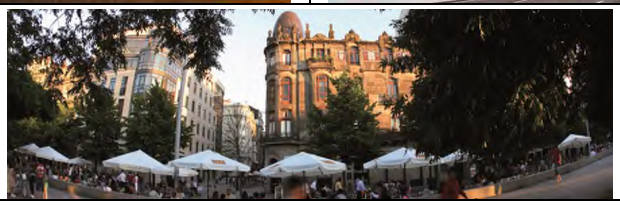
Photos



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ISCB37 Birmingham 2016: Bye Bye!

From Lucinda Billingham (LOC Chair) and Nigel Stallard (SPC Chair)

Attended by more than 600 participants from over 40 countries, the 37th ISCB conference took place in Birmingham, UK from 21-25 August 2016. It was the first time in 13 years that the annual conference was hosted in the UK.

Participants enjoyed a busy and varied programme of oral presentations including 25 invited talks and 245 contributed talks arranged in seven parallel sessions as well as around 200 posters with topics ranging from Observational studies to Adaptive clinical trials and from Small populations to Big data. Highlights included keynote presentations from the President's Invited Speaker, Professor Diego Kuonen, on “Big Data and Data Science in Pharmaceutical Development” and from Professor Sir David Spiegelhalter on The Statistics of Sex.

The conference was preceded by six well-attended excellent pre-conference courses and the final day comprised mini-symposia on Statistical methods in rare diseases and small populations and Strengthening analytical thinking for observational studies (STRATOS) as well as new Students' Day, where students could present their own work as well as hearing talks from established researchers for example on careers in biostatistics. The wide range of talks available meant that many conference participants stayed for the final day.

Birmingham's International Convention Centre (ICC) proved an excellent world class venue for the conference, including a large auditorium for the plenary and invited oral sessions and smaller rooms for parallel contributed talks. The venue also provided room to view posters during the refreshment and lunch breaks, which also provided opportunities to chat to old friends and colleagues as well as meeting new ones from our own countries and around the world. Around the International Convention Centre, conference participants could enjoy this historic part of Birmingham including its canals and iconic new city library, the design of which inspired the conference logo.

The social programme also kept everyone busy. On Sunday evening, the student gathering was attended by 70 young ISCB participants who enjoyed a meal and drinks at All Bar One on the canal side behind the ICC. A ‘lock and key’ game using photos of Birmingham organised by Local Organising Committee members Josephine Khan and Rhiannon Owen proved a fun way for everyone to get to know each other.

The Welcome Reception on Monday evening was held at the Birmingham Museum and Art Gallery in the City Centre. It was a warm evening and ISCB participants gathered for drinks in the Industrial Gallery and the venue’s Edwardian Tearoom was available providing attendees a relaxed informal environment to meet up. Unlike other years, there were no speeches but there was opportunity to look round the collections before disappearing off in groups to the City’s many restaurants.

There were 3 great excursions on Tuesday afternoon and it was a glorious hot sunny afternoon for us all. Some ISCB participants took an open top bus tour of Birmingham ending up at the historic and picturesque Winterbourne House and Garden in Edgbaston. Others took a coach trip to Stratford-on-Avon, the medieval market town that was the birthplace of the famous writer William Shakespeare. A final group of 50 walkers took a coach to the Malvern Hills in Worcestershire to walk along the ridge from the British Camp to highest point of the Beacon, stopping off at the Wyche Cutting for a very welcome drink and viewpoint. The group finally descending into the town of Great Malvern to the Victorian railway station to take a train back to Birmingham and were lucky enough to find the station tea room open to serve them refreshments on the platform whilst waiting for the train.

The social programme was topped off by a wonderful Conference Dinner at the spectacular Edgbaston Stadium which is the home to Warwickshire Cricket Club. We were lucky enough to find a cricket match still underway on our arrival that entertained everyone during the drinks reception. Dinner was followed by speeches and awards from our President and Officers with a final closing rap of thanks from the Chair of the Local Organising Committee. A photo booth kept everyone entertained during the course of the evening and captured some memorable moments and finally the fabulous Subterraneans got everyone up and dancing into the early hours of the morning.

<u>Cindy’s favourite photos</u>:

To see these and all the other conference photos, see Flickr

Conference coffee and poster area

Welcome reception

Bus for the excursion

On the Malvern hills

On top of the Malvern hills

Sir David Spiegelhalter on stage

3 new Honorary Members

New ISCB Honorary Members – Lutz Edler, Michael Schemper, Harbajan Chadha-Boreham

From David W. Warne

At the Conference Dinner at ISCB37 in Birmingham, the ISCB Officers awarded ISCB Honorary Memberships to the following 3 members for their extraordinary contribution to the Society and to the scientific development of biostatistics and its applications in the field of biomedical research.

Honorary ISCB Member 2016

Lutz Edler attended **ISCB1*** in Brussels in May 1979 only 5 months after starting work at DKFZ, and from then on, he has missed only a few conferences, e.g. when they coincided with the COMPSTAT conference of IASC (ISI). He was member of the SPC of the **ISCB17**, Budapest, organised sessions on 'Preclinical Models' at **ISCB20**-GMDS-99 in Heidelberg and on 'Pharmaco-genomics' at the **ISCB26** in Szeged, Hungary.

In close cooperation with late ISCB President, Norbert Victor, he co-organised the big joint **ISCB20**-GMDS-99 Congress in Sep1999 in Heidelberg, with more than 1000 participants, the first time when the ISCB membership passed the level of 800, including 186 members from Germany. Seven years later, he was Chair of the SPC for the **ISCB27** in Geneva, editing with David Warne one of the last paper versions of the ISCB Abstract Book and afterwards, he served ISCB as Guest Editor of the Special Issue of **Statistics in Medicine**.

He served as Secretary of the **Conf SC** from 2011-2013 and worked jointly with David Warne on a thorough revision of the **COSC** Guidelines for organising ISCB conferences in 2013. In addition, he was for several years a member of the **SiRA SC**. From 2009-12, he was a member of the ISCB **ExCom**.

After studying mathematics at the University of Freiburg and basic research on statistics and mathematical modelling, with a PhD thesis on branching processes at the University of Mainz, in 1979, Lutz joined the Department of Biostatistics of the German Cancer Research Center, DKFZ, in Heidelberg. This meant working across all aspects of biostatistics, ranging from pre-clinical studies to large scale clinical trials, from experimental design to interpretation of study outcomes on efficacy and safety, and from methods for computational data analysis to mathematical-statistical modelling.

Currently, 6 years after his 'retirement', he is still engaged in biostatistics for clinical research. Most time he devotes to the EFSA (European Authority of Food Safety) and methodology for human health risk assessment for the regulations of the European Commission.

He has (co-)authored over 400 scientific papers and has co-edited books on statistical methods in risk assessment and 2 special issues on Computational Statistics within Clinical Research in the CSDA journal, with colleagues from ISCB. He served as Associate Editor of biostatistical journals including **Statistics in Medicine**. He was Editor of the **Biometrical Journal** 2012-15 and was involved with the publication of ISCB conference papers, 2015+ in the Biometrical Journal.

*ISCB1: Brussels, May 1979

(Lutz to the left of Sir David Cox)

Michael Schemper joined ISCB at the 1982 conference in Rotterdam (**ISCB3**) and has actively participated in most of next 34 conferences, as speaker, invited session organiser, member of SPCs, twice as Chair of the SPC (1996 Budapest **ISCB17** and 2005 Szeged **ISCB26**), and as Chair of the LOC (2014 Vienna **ISCB35**).

He was **ExCom** member 1996-2000, founded the **NatG SC** in 1996 and was Chair until 2005; he was also an early member of **Educ SC** (drafted Terms of Reference for both SCs), member of the **Conf SC** from 2010, and finally he was proposer of **CADC** and member 2014-2015.

Michael studied Statistics at the University of Vienna, Austria, and earned a PhD in 1977 prior to his engagement as Clinical Biostatistician at the Medical Faculty of the University of Vienna. He achieved a Habilitation in Medical Statistics in 1985 and from this time on, he has supervised numerous Master's and PhD theses in Biostatistics.

He spent the academic year 1987/88 as Visiting Associate Professor at the Department of Biomathematics (MDACC) of the University of Texas in Houston, USA. In 1991 MS became Professor of Clinical Biostatistics at the University of Vienna, where he founded and headed a Section for Clinical Biometrics, now part of a Center for Medical Statistics and Informatics of the Medical University of Vienna. This section recently celebrated its 25th anniversary.

Michael's early scientific interest and research was in nonparametric methods, later in survival analysis, regression modelling problems, and in quantifying explained variation in regression. He has (co-)authored well over 200 papers, partly in medical and partly in biostatistical journals, among them 13 in **Statistics in Medicine**. Some of the papers have been cited several hundred times.

MS frequently reviewed for **Statistics in Medicine** and other journals of biostatistics and also was Associate Editor of **Statistics in Medicine** 2006 – 2013. The statistical methods developed in 3 of his papers (on explained variation in Cox regression, and, avoidance of monotone likelihood in Cox and in logistic regression) have been implemented by SAS as options in 2 of their statistical procedures.

Honorary ISCB Member 2016

Honorary ISCB Member 2016

Harbajan Chadha-Boreham joined ISCB in 1993 and attended her first conference in Cambridge (UK), **ISCB14**. She has been loyal to ISCB since then and has attended 22/24 conferences. She has given contributed and poster presentations at conferences in diverse fields, e.g. Minimisation for treatment allocation; Dose-response relationships; Sample-size estimation; Reporting of risk-prediction models; Growth-curves in paediatric populations, etc. Also, she has frequently chaired sessions at ISCB conferences.

She was an **ExCom** Member: 2001-2004, ISCB **Secretary** from 2005-2008, **Vice-President**, **President**, **Past-President** from 2009-2013. She was the LOC Chair 2002 Dijon, **ISCB23**.

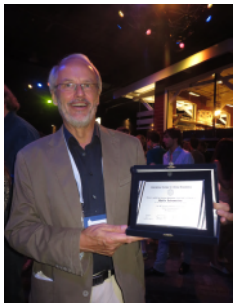
Harbajan has contributed to 4 ISCB SCs: **SiRA SC** Member and Chair: 2000-, 2014-; **Conf SC** Chair/Secretary: Conceived the idea of the SC and was its Chair from 2003-2013, and was lead author of **COSC** Guidelines 2003-2011. These Guidelines laid sound foundations for the long-term growth and success of ISCB by changing the way in which the ISCB conferences are organised.

She was a member of the **Membership SC**, from its creation (2005) to dissolution (2011) and member of the **Epid SC**: Conceived the idea of the SC and was its founding member in 2009, and was a founding member of the STRATOS Initiative 2012-.

Harbajan received her PhD from De Montfort University, UK, on the topic of 'Mathematical and Probabilistic Models for the Growth of Bacterial Populations' in 1982.

She taught in Academia for some years and has worked in the Pharmaceutical Industry (UK, France and Switzerland), where she gained more than 25 years biostatistics experience. She has been involved in both clinical trials and observational studies encompassing many statistical methodologies in over 20 therapeutic areas, which are published in a variety of journals. She has mentored many young researchers during her career and collaborated with internationally renowned clinicians, including membership of Steering Committees and DSMBs.

Currently she is Director of 'Clinical Biostatistics Consultancy' near Dijon, France, and her research interests include risk prediction models in prognostic and diagnostic medicine.



Honorary ISCB Member 2015

Martin is a long-time ISCB member, served as member of the Executive Committee (2005-2008) and several subcommittees (e.g. Statistics in Regulatory Affairs). He studied mathematics and statistics and did his doctoral research at Dortmund University (Germany) and his "habilitation" at Heidelberg University (Germany). He has been a full professor since 1983, first in mathematical statistics at Dortmund University and since 1986, Professor for Medical Biometry and Statistics and Director of the Institute for Medical Biometry and Statistics at the Freiburg University (Germany). Martin has (co-)authored over 250 scientific papers, including about 32 in Statistics in Medicine. He has authored several books and book chapters on statistical methodology, among which "Competing risks and multistate models in R" (Springer, 2012). Martin has organised several statistical conferences, served as Editor of the Biometrical Journal from 2004–2008, and as member of editorial boards (e.g. Statistics in Medicine). In 2012, Martin presented the 21st Bradford Hill Memorial Lecture for the Medical Section of the RSS at the London School of Hygiene and Tropical Medicine, entitled "Hospital-acquired infections – appropriate statistical treatment is urgently needed!" He is currently coordinator of the European Marie Curie training network MEDIASRES with 14 PhD students and corresponding supervisors, many of them also regularly attending ISCB conferences. Indeed, Martin has trained and tutored many MSc and PhD students who have regularly presented their work at ISCB conferences, and he has co-authored at least 13 papers in special ISCB conference issues of Statistics in Medicine.

Emmanuel Lesaffre is currently Professor of Biostatistics and Head of the Biostatistics Department at Erasmus Medical Center in Rotterdam (the Netherlands). In addition, he is Professor of Biostatistics at Leuven University (Belgium) and is also attached to Hasselt University (Belgium). Emmanuel Lesaffre studied mathematics at Antwerp University (Belgium) and wrote a PhD thesis on logistic discriminant analysis. He has (co-)authored over 300 scientific papers focusing on development of new biostatistical tools and rigorous application of these tools to medical applications, he (co-)authored over thirty papers in Statistics in Medicine. He authored several books on statistical methods, most recently a book on Bayesian Biostatistics (Wiley, 2012). He has trained and tutored many students both at MSc and PhD levels and many of them have presented their work at ISCB conferences. In recognition of his work, Emmanuel Lesaffre has held several editorships both from statistical journals (Biometrics & Statistical Modeling) and from medical journals and participated as Organiser to several statistical conferences. Emmanuel Lesaffre has been a long time member of the ISCB and contributed tremendously to the Society. He was Secretary and (Vice-)President from 2001-2008, he served as member of the Executive Committee from 1999-2009, and he was a member of several ISCB subcommittees (Membership, Conference Organising, Education, Student Conference Awards) and initiated the subcommittee stimulating application of biostatistical methods in Dentistry research. Finally, Emmanuel Lesaffre was chair of the Scientific Programme Committee of the ISCB conference in Montpellier (2010).

Honorary ISCB Member 2013

Honorary ISCB Member 2011

Hans Van Houwelingen is a "distinguished biostatistician and has given service of exceptional value and duration to ISCB," as required by the constitution. Although in retirement since 2007, he has remained very active and we see him every year at the ISCB conference. Hans' contributions to Biostatistics are well-recognised and the Biometrical Journal 52 (2010) is dedicated to his "40 years in Biostatistics" where it states, "He is considered to be the father of biostatistics in the Netherlands and to put Dutch biostatistics on the map, both nationally and internationally." At the ISCB Maastricht in 1989, Hans gave a lecture on "predictive value of models" and "shrinkage and validation of prognostic models" and the related paper, which appears in Statistics in Medicine, brought him international recognition. It is one of the most cited papers. Therefore, we can see why the ISCB has a special meaning in Hans' life and career. Hans has prolific publications of very high standard in many research areas, including Bayes methods, prognostic models, meta-analysis, survival analysis, genetics and bioinformatics in genomics. His interest lies in applications of the methods not only in medicine but also in agriculture. He has one of the longest lists of publications (11) of ISCB conference papers in Statistics in Medicine. Hans has been a regular contributor to the ISCB in significant ways for well over 20 years: Member of the Executive Committee: 1993 – 1996 for two terms, ISCB Scientific Programme Committee Member (3 times): Stockholm (2001); Leiden (2004) & Alexandroupolis (2007), Chair of Local Organising Committee, Leiden (2004), Mini-symposium: Genomics based diagnosis and prognosis, Szeged (2005), Pre-conference course: Assessment of predictive performance by cross-validation (in collaboration with Martin Schumacher), Geneva (2006), Invited session papers (2 times): Data analysis when the number of predictors (p) greatly exceeds the number of cases (n), Leiden (2004) and Surrogate markers in clinical trials, Alexandroupolis (2007).

Stephen Senn is one of the most faithful ISCB members: He attends here his 25th annual meeting, has given many very exiting lectures (among them the keynote lecture in 2003), he contributed 10 papers to the congress issues of Statistics in Medicine, and he has taught several pre-conference courses, as well as courses in target countries. Stephen became an ordinary ExCom member in 1991 and served as Secretary from 1992 to 1995. He also served the Society in many other functions: He was member of several Scientific Programme Committees (SPCs, once, Dijon 2003, acting as Chair), editor of the Dijon congress issue of Statistics in Medicine, LOC member for ISCB15 in Basle, and Secretary of the SC "Statistics in Regulatory Affairs". As Stephen is accepted worldwide – both in academia and the pharmaceutical industry – as an outstanding biostatistician, there is no need to enumerate his scientific merits here.

Honorary ISCB Members 2009

John Whitehead's list of merits and services to ISCB is as long as that of Stephen; he is without any doubt one of the most loyal members since the society was established: John attended the first ISCB meeting 1979 in Brussels and most of our meetings after that, he presented a large number of papers, he taught several ISCB courses and he contributed the highest number (12) of articles to our congress issues of Statistics in Medicine. Apart from our first two Honorary Members, John has been the ExCom Member with the longest period of service; this period of twelve years includes four years as Treasurer, two years as President and three years as Vice-/Past-President. John also served the Society in many other functions, e.g. as member of several subcommittees, chair of the Student Conference Awards committee, member of SPCs and member of the LOC in 2003. John's reputation as outstanding scientist is undisputed. Therefore, I would like to mention only two of his prominent merits: his role as driving force and teacher in the Biostatistics Master programme in Reading, and his widely used monograph on sequential trials.

David Warne is a longstanding and very faithful ISCB member. He has been the editor of the Newsletter Editor since 1992-3 and served eight Presidents (Claude Chastang, Jorgen Seldrup, Marc Buyse, Karsten Schmidt, Simon Day, Grazia Valsecchi, John Whitehead, Emmanuel Lesaffre). This is a quite demanding task requiring a lot of secretarial but also communication skills. It has been repeatedly confirmed that The Newsletter constitutes an important link for the ISCB members. In his role as Chair of Communications he has also explored various other possibilities to improve the communications among ISCB members. For instance, he installed the ISCB emailing system thereby creating various dedicated email groups. He also contributed to the development of the ISCB Website. Further, he is the chair of the Subcommittee on Communications and is a member of the Subcommittee on Conference Organising. Finally, he Organised recently one of the most, if not the most, successful ISCB meetings in Geneva. Not only the scientific and social programs were excellent, he also realized a substantial financial profit for the Society. For all of these reasons, the Officers recommend David to receive the status of honorary membership of our Society.

Honorary ISCB Members 2007

Jorgen Seldrup was the Newsletter Editor in 1985 & 1986 and in 1990 & 1991, Scientific Secretary from 1987 to 1990, Vice-President in 1991 & 1992, President in 1993 & 1994 and Past-President from 1994 to 1996. In total, he served the Society in the Executive Committee for a much longer period (1984 to 2000). Jorgen has been one of the most loyal ISCB members since The Society has been established in 1979. He has been member of various ISCB subcommittees but is especially known for chairing the Subcommittee on Regulatory Affairs for many years, where the main task is the preparation and submission of comments on the draft regulatory guidelines. Further, he has served in various nominations committees. He is on the Scientific Committee of the meeting in Alexandroupolis where he is also the Organiser of an invited session on "vaccines". For all of these reasons The Officers recommend Jorgen to receive the status of honorary membership of our Society.

Book Review by Maria de Ridder (NL)

Robert D. Gibbons, Anup Amatya	Statistical Methods for Drug Safety	CRC	2015	9781466561847

The book starts with a nice preface, with a touch of scepticism of a statistician entering the area of pharmaco-epidemiology. Doing several studies on drug safety, starting with research about the possible adverse event of nausea related to the use of Halcion (a short-term hypnotic) after an incident involving President George Bush Sr. at a banquet, the first author of this book acknowledged the statistical challenges for this type of research questions and the need for developing good methods. Observational data is an important source of information, with 'confounding by indication' as a known complicating factor. The importance of sound studies on drug safety is obvious: both unrecognized risks as well as false safety concerns may have big implications for public health.

The first chapters handle basic statistical concepts and methods, not specific to analysis of drug safety. Because using longitudinal data is quite common, one chapter is devoted to multi-level models.

Chapter 4 is focused on methods for drawing causal inference from observational data: propensity score matching, marginal structural models, use of instrumental variables and differential effects. As throughout the book, all these techniques are illustrated with a data example, and opportunities and limitations are discussed. For inexperienced readers, more information will be needed to apply the methods, for which several references are given.

A source of information very specific to drug safety are databases with spontaneous reports of adverse events. Several countries have such a database, of variable quality regarding completeness, coding and details. There are also some large international registrations. It is obvious that this type of data requires specific analysis methods. In chapter 5 these methods are discussed, ranging from the straightforward proportional reporting ratio (using the cross-table 'drug of interest/other drugs' versus 'event of interest/other events'), to Bayesian lasso logistic regression. In a short discussion at the end of the chapter the authors emphasize that these techniques are useful to screen for possible drug-adverse events relations ('signal detection') but can never be sufficient to do drug safety research. Because of the complex and changing structure of the data source, methods are still being developed.

Then the book jumps to the topic of meta-analysis. Those methods extensively described and explained include: fixed and random effects meta-analysis, maximum marginal likelihood, Bayesian meta-analysis and using a confidence distribution framework. This is the only chapter which provides some software code. There is one example of using SAS Proc NLMixed for the maximum marginal likelihood method to analyse clinical trials of which some have zero events in one of the treatment arms. WinBugs code is given for a Bayesian meta-analysis on RCTs estimating the risk for myocardial infarction with use of rosiglitazone, a well-known case of a drug related adverse event.

Almost all examples in this chapter concern meta-analyses of clinical trials, with results summarized in two by two tables. Unfortunately this is mostly not suitable for observational studies.

More focused again on drug safety are ecological methods. These involve methods using aggregated data on group level. For example, in a population the rate of an event over time is known and these are related to drug utilization data, or the introduction of a new drug. Different types of time series methods and change-points analysis are discussed and applied to data of 20 years of mortality rates related to opioid poisoning. Unfortunately, all these methods give slightly different conclusions and a comparison between them is not provided. Next, an application of a mixed-effects Poisson regression model is given, on data of SSRI (a group of antidepressants) use and suicide rates at county level in the United States.

In Chapter 8, discrete-time survival models are discussed. Data on survival in registration databases (e.g. claims data) can be clustered in time intervals, and these parametric survival models could be more efficient in this situation than Kaplan-Meier estimates or Cox models. A drawback is the lack of some description of how the data should be organised, which software can be used and some code for these kinds of analyses.

Chapter 9 deals with 'research synthesis'. In the introduction it is described as 'reanalysis of the complete original data' of different studies, in contrast to meta-analysis, which combines effect sizes. The more commonly used term 'individual patient data meta-analysis' is not mentioned. In this chapter three-level (studies, patients, measurements) mixed effects regression models are discussed. All examples are about combining data from RCTs.

The chapter "Analysis of medical claims data" is described as "the heart of this book". After some information about this type of data and observational data in general is provided, suitable designs and analysis methods for claims data are discussed. It is questionable whether this chapter is the most suitable location for these descriptions of methods and reporting of two simulation studies illustrating the differences between fixed-effects and various mixed-effects models. The application of many methods, all to analyse the same research question using data of a large claims database, completes this chapter.

Finally, some 'methods to be avoided' are briefly presented. Notable are the warnings for doing multiple comparisons without any adjustment or reporting non-significant results with risk above one as a safety concern.

In summary, this book gives a broad overview of different analysis methods for drug safety. Methods are mathematically described, partial information is given on which software to use and examples from the pharmaco-epidemiological literature are numerously provided.

The structure and presentation could have had some more attention. Several tables and plots would gain clarity with a more informative title and legend. When an item comes up in several chapters, the link between these discussions could be more clear. However, the book is inspiring, both for applying the described methods as for doing more research to develop and improve methods.

Book Review (1) by Beth Stuart (UK)

Tie-Hua Ng	Noninferiority Testing in Clinical Trials: Issues and Challenges	CRC	2014	9781466561496

This text aims to provide an overview of the key issues in the design, conduct and analysis of non-inferiority trials. The aim does not appear to be to give definitive answers on the "right" and "wrong" way to undertake these sorts of studies but rather to guide the read through some of the important considerations in this area.

Chapter 1 sets out the non-inferiority and equivalence trial and how they differ. It explores the equivalence and non-inferiority margin, reviewing the literature on how it might be chosen. Ethical issues are discussed in the context of choice of control, particularly the choice of placebo versus active control and the implications this may have for sample size calculations. Most of the examples in the book are based on the active control scenario.

Chapter 2 sets out how to choose the non-inferiority margin and how to determine the effect size in the context of a mean difference. It talks about issues of constancy and assay sensitivity and whether adjustments to historical data may be justified or even necessary. Chapters 3 and 4 are quite short and review these same concepts for a mean ratio/hazard ratio and binary outcome respectively.

Chapter 5 covers hypothesis testing. Using an alpha of 0.025, the author discusses the merits and drawbacks of the fixed margin and synthesis methods, including the impact on efficacy and the type I error rate.

Chapter 6 explores the option of switching between non-inferiority testing and superiority testing. Although attractive option, allowed by many regulatory authorities without a multiplicity assumption, the author sets out why it is important to also consider the false discovery rate.

Chapter 7 turns to meta-analysis as a method for estimating the effect size. It covers both the fixed and random effects models before looking at the implications for non-inferiority testing, the impact of the constancy assumption and whether discounting may be appropriate.

Chapter 8 extends the issues already discussed to situations where there are three groups. Chapter 9 considers the existing regulatory guidances.

Chapter 10 sets out the differences between Intention to Treat and Per Protocol analyses and, from section 10.5 onwards, the specific issues regarding these approaches for non-inferiority trials. It discusses the reasons why ITT analyses may be considered non-conservative in this context but also explores the limitations of PP analyses.

Chapter 11 provides a worked example of some of the issues discussed in the text and Chapter 12 gives a final review of some of the issues and challenges set out in the book.

Whilst the author gives a good overview of the current issues, there are some parts of the book that feel as though they may date. Some of these issues represent areas of ongoing research and thus the field may move on from that depicted in the book in the coming months and years. Similarly the chapter on regulatory guidance reflects the current position but of course this is subject to change. However, the book represents a good, clear and fairly concise introduction to the key issues and considerations that should be thought through by anyone considering undertaking a non-inferiority trial.

Book Review (2) by Beth Stuart (UK)

Chul Ahn, Moonseoung Heo, Song Zhang	Sample Size Calculations for Clustered and Longitudinal Outcomes in Clinical Research	CRC	2015	9781466556263

This book aims to be a useful reference for those of us who are frequently asked "how many people will I need to recruit?" The considerations are more complex in the context of clustered and longitudinal data and this text provides a useful reference, especially for those circumstances where existing sample size calculation software is insufficient and the statistician may need to make adjustments to obtain a sample size appropriate to the specifics of study design.

Chapter 1 provides an introduction to sample size calculations for independent outcomes, with formulae and clear worked examples. The text encourages readers not only to think about the calculation itself but also the assumptions that underlie it.

Chapter 2 begins the consideration of clustered designs by looking at clustered outcome measures. The chapter covers the rationale for accounting for clustering and then gives appropriate equations for calculating the sample size for continuous and binary outcomes with equal and unequal cluster sizes. For one sample clustered outcomes, formulae are presented for 3 different weighting schemes: equal weights to clusters, equal weights to observations and minimum variance weights. The chapter finishes with a consideration of the implications of different types of clustered designs – e.g. parallel, crossover and stepped wedge.

Chapter 3 focuses on repeated measures designs that report summary outcomes and the implications for the sample size of the correlation between measurements. The chapter begins by setting out the most common correlation structures used in repeated measurement studies and assumptions about missing data, which is more common in longitudinal designs. The chapter then sets out formulae for the analysis of the difference score, the difference score adjusted for baseline, the difference in the rate of change across time with and without adjustment for baseline, and the time averaged difference – again with and without adjustment for baseline. The chapter finishes with a brief consideration of the implications of multiple treatment groups and summary statistics for binary outcomes.

Chapter 4 looks at sample size calculations using Generalised Estimating Equations. It begins with a brief overview of GEE. It then give details on the equations and assumptions required to compare the slope and the time averaged difference for continuous outcomes including the implications of correlation structures, missing data and multiple groups. The same consideration is then given to binary and count outcomes.

Chapter 5 turns its attention to correlated outcomes from two-level randomised trials, where participants may be clustered in groups (households, clinics, etc.) or where repeated measurements are clustered within participants over time. The chapter sets out sample size calculations for balanced and unbalanced allocations for different randomisation strategies and designs, including factorial designs. Both continuous and binary outcomes are considered.

Finally Chapter 6 explores the calculations required for 3-level randomised trials. These models represent an extension of those presented in Chapter 5.

This text provides a useful reference for those who wish to calculate the sample size for a clustered design. Although the formulae and issues presented here are not new, it is very helpful to have them all collated in one book with clear and accessible examples and some thoughtful reminders of key considerations.

Book Review by Susanne Urach (AT)

Scott M. Berry, Bradley P. Carlin, J. Jack Lee, Peter Muller	Bayesian Adaptive Methods for Clinical Trials	CRC	2010	9781439825488

As Bayesian methodology is receiving more and more attention by biostatisticians, this book serves as an extensive summary of current Bayesian adaptive methods in the different phases of a clinical trial design. Very different methods concerning the objectives of Phase I-III are investigated in a clearly arranged way by disaggregating the decisions into different steps of an algorithm making the approaches easy to understand and apply yourself. The theoretical designs are illustrated by many real life applications testifying to the experience the authors have in providing adaptive clinical trial design in pharmaceutical and medical device research and development. The clinical trial methodology focuses on probability calculations using prior information and Bayesian updating while still controlling for frequentist error rates and less on decision theoretical designs based on a utility function.

Chapter 1 (Statistical approaches for clinical trials) addresses the controversy between the frequentist and the Bayesian approach to statistics and illustrates the advantages of the Bayesian methodology using predictive probabilities, adaptive randomization and seamless Phase II/III trials with examples from drug and medical device development. Nevertheless these trial design characteristics are also achievable in a frequentist framework and a comparison with the competitive approach is somehow missing leading to a one-sided advocacy of Bayesian clinical trial designs.

The arrangement of the different subsections in Chapter 2 (Basics of Bayesian inference) seems a bit arbitrary, but provides a good overview of different Bayesian methodology. Chapter 2 introduces the basics of Bayesian inference beginning with the obligatory Bayes' theorem and the calculation of the Bayes factors. Then a rather technical excursion to Bayesian computation is undertaken, i.e. Markov chain Monte Carlo (MCMC) methods typically used to numerically evaluate the integral in the denominator of Bayes' theorem. As sampling algorithms for MCMC the Gibbs sampler and the Metropolis Hastings algorithm are discussed, but also implementation problems like convergence diagnosis and variance estimation are mentioned. Afterwards Bayesian hierarchical modeling and Bayesian methods for designing clinical trials are illustrated using the WinBUGs software which can be called from R using the BRugs package. The experimental design decisions discussed should work as the foundation for the later chapters where these methods are used in the different phases of clinical trial design. In the design stage of a clinical trial the authors see the application of Bayesian methods as less controversial because also in the frequentist framework the trial designer must have some pre-existing knowledge regarding the likely effect of the treatment and its variability. Bayesian methods for designing clinical trials involve e.g. stopping for futility or efficacy using predictive probability and indifference zone methods. At the same time the frequentist operating characteristics are derived by simulation. The advantages of the Bayesian over the frequentist approach when handling multiplicities, interim looks and delayed responses are discussed, but the authors have to admit that these only hold if there is no interest in the long-run frequency properties of the procedures. For prior determination the authors differ between analysis and design prior where the former might be less informative to win over sceptics. As trial results may be sensitive to the choice of prior, a community of priors consisting of sceptical, enthusiastic and non-informative priors are recommended. Beside these Bayesian probability methods which base decisions entirely on the posterior distributions of the model parameters, Bayesian decision theoretical approaches to incorporate costs in the decision making are briefly mentioned. Although Bayesian decision theory can be extremely helpful to make decisions about the cost effectiveness of a drug compared to control, the authors warn that these results depend crucially on the precise costs selected.

Chapter 3 (Phase I studies) explains how Bayesian methodology helps to solve "early phase" problems concerned with establishing safety and studying the pharmacokinetics and pharmaco-dynamics of a drug. Here the emphasis is put on finding the maximum tolerated dose (MTD) in a dose escalation trial where the risk of toxicity has to be balanced with the risk of treating patients at ineffective doses. The traditionally rule-based designs are compared to the model-based designs for determining the MTD. The former, although easy to implement, are criticized for being inefficient as they rely on information from the current dose level only and the target toxicity level (TTL) is only implicitly defined. On the other hand model-based designs specify in advance the TTL and the monotonic dose-response relationship between the dose and the probability of dose-limiting toxicity for patients treated at that dose. Here the aim is to find a suitable quantile of the dose-toxicity curve, i.e. a probability of DLT at a specified TTL. The parameters of the models for the dose -toxicity relationship are estimated with the Bayesian posterior distribution using all the data. As examples for model-based approaches the continual reassessment method (CRM) and the escalation with overdose control (EWOC) method are given. The advantages of using the Bayesian model-based designs are according to the authors that more patients are treated at the dose closest to the MTD. As CRM allows jumping over multiple dose levels, either mechanistic modifications or the EWOC method are suggested to avoid safety issues. In case the outcome is not binary, the CRM algorithm can be readily extended to time-to-event (TITE) outcomes which base the design on a parametric event time model. If the TTL cannot be reliable identified, then the authors suggest to use approaches based on toxicity probability intervals rather than on target levels or to extend the traditionally binary classification into an ordinal scale over four sub-intervals of toxicity probabilities. Especially in cases that the efficacy does not increase with the dose, Bayesian adaptive methods could combine the goals of phase I and II using a joint probability model for efficacy and toxicity. Here the aim is to find the highest effective and lowest toxic dose as is done using the Efftox method by Thall and Cook. To investigate multiple drugs in a combination therapy the authors discuss the use of a multi-parametric model for the toxicity probabilities arising in the various dose combinations. As "bivariate" CRM methods the approaches by Yin-Yuan to combination dose-finding designs using the Gumbel model and by Thall et al. using a 6-parametric bivariate logistic model are described.

In Chapter 4 (Phase II studies) the focus shifts from trials studying safety to examining the efficacy of the drug and evaluating if further development would pay out. Single-arm Phase IIA studies serve to screen out ineffective drugs, whereas multi-arm phase IIB trials compare the efficiency of the new treatments versus the control to select the most promising treatment for Phase III. As multi-stage designs allow stopping for futility in case of inefficacious drugs, they are especially helpful to minimize the expected sample size under the null hypothesis or to minimize the maximum sample size of the trial. In contrast to the Phase III trial designs studied in Chapter 5 the phase IIB trials are smaller and have larger Type I error rates. Control of the false-positive rate is seen as less important than control of the false-negative rate because any active treatment should not be missed whereas the final verdict of the effectiveness of a drug is left to the Phase III trial. Due to low sample sizes no head-to-head comparison between treatment arms is possible and only one-sample hypothesis testing in each arm separately is done. As the primary endpoint in this phase is often binary (response/no response), pick-the-winner designs based on ranking and selection methodology like the SWE approach are often employed. This frequentist method has the disadvantage that it only picks the treatment arm with the best observed outcome as the winner regardless of whether all, some or none of the arms are efficacious. According to the authors Bayesian approaches using multi-stage designs may be superior because the information gained in the interim analyses lead to better statistical properties. Although the possibility to perform interim analyses in the frequentist framework is briefly mentioned, it is claimed that the sample size always needs to be specified in advance which is not true when using spending functions. Additionally many adaptations are possible at interim when using a combination function approach. As Bayesian adaptive methodology the predictive probabilities introduced in Chapter 2 are now applied to a Phase IIA trial with a binary or time-to-event endpoint. For the authors the main advantage of using Bayesian inferences in sequential designs is that as long as the stopping rule and the parameters are independent a priori, the number of interim looks does not affect the outcome avoiding "frequentist stopping bias". For a Phase IIB multi-arm clinical trial adaptive randomization and dose allocation increases the assignment of patients to more promising treatments/doses. If there is a non-monotone dose-response relationship, the aim is to find the dose with highest efficacy among a range of safe doses which is the optimal biological dose. In this context the authors suggest dose-finding methods based on jointly modeling toxicity and biomarker response. The hierarchical models introduced in Chapter 2 in the realm of meta-analysis can also be used to borrow strength across related trials in phase II, e.g. using all data across closely related subpopulations to calculate posterior probabilities and decide to stop for futility or not. At the end of Chapter 4 two Phase II adaptive trials (BATTLE, I-SPY 2) serve as examples of ongoing high-profile trials where adaptive randomization, hierarchical modeling and sequential stopping are applied.

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Chapter 5 (Phase III studies) deals with confirmatory clinical trials, i.e. large randomized controlled clinical trials for definitive assessment of the efficacy of the drug. For regulatory authorities type I error control in this phase is still paramount and the chapter deals with the multiple issues arising due to adaptations such as stopping for efficacy or futility, dropping of treatment arms and seamless phase II/III trials. The Bayesian analyses using predictive and posterior probabilities are adjusted to have adequate frequentist properties rendering the Bayesian approach somehow redundant. This paradigm clash is also addressed, but according to the authors could only be resolved by changing the regulatory structure of judging clinical trials not using type I error, but fully Bayesian notions of utilities and decisions. Nevertheless decision theoretic clinical trial design are seldom used in practice due to the difficulty of specifying a good utility function and deciding whose utility is relevant.

At last Chapter 6 (Special topics) is dedicated to the incorporation of historical data, equivalence studies, multiplicity and subgroup analysis. To use information from historical controls in the standard hierarchical models approach, the likelihood, prior and hyper-prior determining the degree of borrowing have to be specified. Simulations of type I error and power determine how tightly the hyper-prior can be set such that borrowing is still effective and the Type I error is not too high. Another approach in the book to incorporate historical data is with the help of power prior models where a conditional power prior for the unknown parameter is defined which is used to calculate the conditional posterior distribution. For the conditional power prior the initial prior is multiplied with the likelihood function of the historical data taken to the power of a parameter which defines the amount of borrowing. For equivalence studies the two one-sided test procedures strike the authors as quite unattractive because it first reformulates and then swaps the hypotheses while Bayesian solutions involving the Bayes factor or the indifference zone approach can be naturally adopted. In case of multiple testing hierarchical modeling is also suggested as a way to determine how much correction is required. For subgroup analyses the authors suggest Bayesian methods for modeling the interaction effect respectively Bayesian decision theoretical approaches when to report efficacy of the overall population or some subpopulation.

Overall the book is a useful overview of how to apply adaptive Bayesian designs in the different phases of clinical trials containing many real life examples where the methods could or have been used to obtain an optimal design. Not only the mathematical foundations are explained in a clearly arranged stepwise way, but also how to implement the different methods in R and other software products.

Book Review by Stephen Walter (CA)

Byron Jones, Michael G. Kenward	Design and Analysis of Cross-Over Trials (3rd ed.)	CRC	2014	9781439861424

This text has had a long shelf life, with its first edition appearing in 1989. Even at that time, the authors commented on the "large and growing literature" on cross-over trials, and now this third edition attempts to catch up on developments in the area (since the second edition, in 2003).

After a short introductory chapter, Chapter 2 goes into extensive detail about 2 x 2 trials. This chapter is unchanged from the earlier editions, and it occupies a substantial portion of the whole book (with 93 pages, 18 Figures and 41 Tables). Chapter 3 discusses higher-order designs (more than two treatment sequences, and/or more than two treatment periods), while extensions to three or more treatments appear in Chapter 4.

Revisions to Chapters 5 and 6 have resulted in more emphasis on methods for continuous and discrete data, including very small trials. Bioequivalence trials are briefly in a relatively short Chapter 7.

The major addition to the third addition is seven new chapters presenting case studies. Several of them deal with sample size re-estimation (for average bioequivalence and in proof of concept studies), and the others discuss non-linear dose-response relationships and optimal dose estimation.

As my personal benchmark to identify the target readership for this book, I noted that the authors state that the major Chapter 2 on 2 x 2 trials should be "accessible to the less statistically experienced", and that the material "is at a fairly elementary level". However, it is not completely clear from this what the intended audience might be, specifically what level of "experience" might be required, or what the authors might regard as elementary. This reader found numerous advanced elements in Chapter 2 such as: extensive algebraic derivations; convex hulls; presentation of expected mean squares in ANOVA tables, without any general explanation; aliasing; Gibbs sampling; bivariate rank sum statistics; and matrix algebra equations. All of this will certainly be challenging to most "less statistically experienced" readers (non-statisticians?), and I found it a stretch to classify this material as "elementary".

On the other hand, some "more statistically experienced" readers (statisticians?) will find material of this kind an invaluable reference text, providing many details of theory and analysis that might be hard to find elsewhere. Some of these readers will occasionally disagree with the authors approach or their conclusions. For instance, Jones and Kenward regard a *p*-value of 0.043 from a Shapiro-Wilks test as providing "some evidence" of non-normality in one study group, while $p = 0.144$ in the other group is given without comment, and without discussion of the power of this particular test. Similarly, elsewhere a subject is removed from an analysis simply because he is an outlier, but without further investigation as to why.

Analysis is recommended using R, or current features of SAS procedures *glimmix* and *genmod*. Detailed codes are often provided in the text, but unfortunately some of the Figures showing screenshots of this software are only legible with difficulty, even with a magnifying glass! I also noticed some legibility issues in some Figures elsewhere (e.g. Chapter 2), with very small fonts and sometimes unhelpful aspect ratios.

It is always helpful to consider the competition. In this case, I have used Stephen Senn's Wiley text (*Cross-over Trials in Clinical Research,* 2002) for some time. It is aimed at a somewhat different audience, specifically clinical investigators or statisticians without previous experience with the cross-over design. Because of Senn's apparently lower calibration of required "statistical experience" (compared to Jones and Kenward), his book is more immediately accessible as a way to "get started", while also covering the essential theory and applications in some detail. Senn also deals with certain practical aspects such implementation in multiple clinical centres, blinding, amongst others, which receive less attention in Jones and Kenward.

However, Jones and Kenward has now been comparatively brought up to date since the 2002/3 appearance of both their second edition and that of Senn. It can therefore be recommended as a more contemporary review of the cross-over waterfront, particularly for advanced readers. On the other hand, any potential readers who are "less experienced" should be aware of the significant technical challenges they will face in digesting this book.

Book Review by Per Kragh Andersen (DK)

Daniel Commenges, Helene Jacqmin-Gadda	Dynamical Biostatistical Models	CRC	2015	9781498729673

The properties of this book may be summarized in two words: rich and concise. It is rich because it covers a lot of material as reviewed below, and it is concise by doing this in less than 400 pages.

The two authors are from University of Bordeaux, France and the text builds to a large extent on research conducted there. It is stated on page xxxi that the book has another six co-authors from the same biostatistics team in Bordeaux. The book has two main streams: models for survival and event history data and models for longitudinal data. These topics are treated initially in separate chapters but in Chapters 8 and 9 the two topics 'converge' as these chapters deal with joint models and with causal inference based on stochastic processes.

The initial Chapter 1 mainly presents three practical examples that are used for illustration throughout the text: The PAQUID study on dementia conducted in the Bordeaux area, the ALBI trial in AIDS, and a data set from a prospective study in colorectal cancer from Barcelona, Spain. Chapter 2, the first chapter in the part of the book entitled 'Classical Biostatistical Models', provides a crash course in statistical inference methods including optimization algorithms. Thus, likelihood methods and criteria for model choice like the AIC are briefly discussed. A remark could be that surprisingly little is said about the bootstrap, but the chapter is brief and to the point. Chapter 3 provides a basic description of survival analysis and includes the topics that most such reviews would contain, plus a brief section of so-called 'degradation models' where the event time is a first passage time of a continuous stochastic process. In a similar vein, Chapter 4 introduces models for longitudinal data, including classical linear mixed models, generalized linear mixed models, and marginal models. The chapter concludes with brief sections on incomplete data and modeling strategies. In particular, the latter section gives some useful advice based on the authors' experience.

The second part of the book is entitled 'Advanced Biostatistical Models' and builds on Part I. Chapter 5 extends the previous chapter and discusses nonlinear and multivariate linear models, as well as latent class models. Similarly, Chapters 6 and 7 extend Chapter 3 and discuss more advanced models for survival and event history data, including (Chapter 6) relative survival, competing risks, and frailty models. In the sections on frailty models, special attention is paid to the situation where a random effect is shared between a recurrent event process and a terminating event and where important methodological developments have taken place at the biostatistics team in Bordeaux. Chapter 7 deals with multi-state models (except the competing risks model which was treated in the previous chapter) and includes an in-depth discussion of the illness-death model with interval-censored data where, again, important development has been achieved by the authors.

As mentioned above, the two lines of models come together in Chapter 8 about joint models for longitudinal data and survival data. The main modeling approach is that of shared random effects which can either be a quantitative 'frailty' or a categorical 'latent class'. These two types of models are nicely contrasted in a separate section. The second to last Chapter 9 is in some respect the most interesting chapter of the book since it deals with a topic not covered by other books. The topic is the dynamic approach to causality and builds again on the authors' own previous research. The now classical approach to causal inference based on potential outcomes is criticized via a number of important arguments and stochastic systems are put forward as an alternative. Some practical applications are given but more experience with the use of this idea is needed, and in the current view of the present reviewer, both approaches to causal inference seem to have their place in the toolbox of a biostatistician.

In the final Chapter 10, useful code in both SAS and R is provided for most of the methods presented in previous chapters.

In conclusion, this is a very well-written book that manages to cover a lot of ground in a remarkably succinct way. In addition to sections including more standard material on survival analysis, on the one hand, and longitudinal data on the other, both sections giving useful practical advice and sections discussing entirely new material are found. I can highly recommend the book.

Book Review by Erik Cobo (ES)

Cosmatos,Dennis, Chow,Shein-Chung (eds.)	Translational Medicine: Strategies and Statistical Methods	CRC	2008	9781584888727

Too many promising agents in basic research tend to fail at the patient level. My scepticism led me to suspect that quality and confirmatory methods that are compulsory at the latter phases have to be applied in early development. But ISCB gave me the chance to review this book, and I have learnt how statistics can facilitate communication between different disciplines and departments, which in turn expedites transitions along the research and development pipeline.

It contains 10 chapters that pretty much stand alone. The first two are introductory, and they describe the need for Translational Medicine (TM) approaches through the development process as well as key ideas for guiding this process, mainly linking different disciplines. Next Subsequent chapters follow the natural order from discovery research to final implementation to intermediate validation. Chapter 3 begins by addressing assays at the sub-cellular level and finishes with an introduction to trial simulation. Chapters 4 and 5 focus on biomarker development and enrichment trials, explain regulatory principles and provide a macro for simulating adaptive trials. Chapter 6 is probably the most interesting chapter, dealing with animal versus human statistical models in an elegant, conceptual and formal way. In contrast, Chapter 7 merely provides an overview of classical bootstrap methods without practical TM examples. Chapter 8 is more practical, with examples of model evaluation that follow relevant FDA advice. Chapter 9 applies Bayesian methods for translating efficacy between different ethnic populations. Finally, Chapter 10 makes an attempt to facilitate a two-way translation between Western and Chinese medicine.

I anticipate that future versions of the book will complete some chapters, such as the second and the seventh, with examples of TM, program macros or comments on regulatory guidelines. In addition, Chapter 10 may be replaced with one that specifically focuses on the final transition from research laboratory to the patient's bed.

In summary, I would reiterate that I have learnt that statisticians can do more than be co-workers in specific disciplines: they may facilitate scientific communication among different departments in order to speed up the translation of new agents throughout the R+D process. This is no surprise; after all, statistics is the common language behind empirical scientific fields.

Ian C. Marschner	Inference Principles for Biostatisticians	CRC	2015	9781482222234

As someone who teaches on a one year MSc in Medical Statistics I have always struggled with what level of inference theory needs to be presented to students so they can be effective biostatisticians. This is further complicated as our usual student intake is quite varied ranging from clinicians wishing to upgrade their research skills to mathematics and statistics undergraduates looking to undertake PhD studies in the future. The point was bought home forcefully to me recently when a student undertaking their MSc research project referred to knowledge needed to be a "real statistician" when I was quizzing them on some element of inferential theory. They clearly did not see the necessity for that level of knowledge to effectively do their job!

With that context in mind I was naturally drawn to Marschner's new book. The first thing to like about it is the size! No weighty tome to fill students with dread – I need to know all of that (or more typically I need to do all those problems!). The book forms the core resource for a module in statistical inference as part of an innovative Master's course in biostatistics delivered via e-Learning across a number of Australian Universities (http://www.bca.edu.au/). Students on this MSc are required to take preliminary courses in mathematics (calculus and some matrix theory) as well as modules in probability and distribution theory. The reason I mention this is that some student in other courses may lack this preparation and hence will require a specific probability course or integrated probability and inference module. The relative slimness of the volume does mean in places subjects are dealt with a little tersely and deeper ideas tend to be skirted over. The biggest omission due to the size of the volume is in explanatory graphics for some key ideas such as the various likelihoods – these tend to appear in the specific extended examples in each chapter. The volume is also light on providing a lot of statistical computing but I think instructors here can supplement this element by directing students to use their computing tools (e.g. R, Stata or SAS) in solving the end of chapter problems.

With those background issues out of the way the book is organised in eight (8) chapters. Chapter 1 is a quick review of probability and random sampling. Chapters 3 to 6 cover the core topics in classical frequentist inference: estimation (chapters 2 and 4), likelihood (chapter 3), estimation methods (chapter 4) and hypothesis testing (chapters 5 and 6). Chapter 7 is an introduction to Bayesian inference and chapter 8 is special topics. The book is completed by appendices covering background for common distributions, simulation tools and a list for further reading.

Chapter one introduces the idea of statistical inference and reviews common concepts in probability from the frequentist perspective. The probability concepts are reviewed concisely reflecting the assumed background of the students including the use of matrix notation in defining the multivariate Normal distribution. The concept of a random sample is introduced and linked to the sorts of sampling designs one observes in biostatistics (prospective, retrospective and cross sectional). The central idea that the data can be considered as being generated by a data generating mechanism that can be expressed as a probability model occurs here. There is a short section on sampling biases before the two main sections. The first deals with sampling variation and how it can be measured via the assumptions of the data generating probability model. Finally, the chapter ends with a section on large samples that introduces the central limit theorem and law of large numbers. As it typical throughout the book the end of chapter exercises are a nice mix of "pen and paper" and simulation based questions to aid understanding. R code is given at the end of the book so that students can run the simulation exercises.

Chapter 2 deals with estimations concepts. After first defining statistical models in general it moves on to parametric statistical models used to describe data from random samples. Defining estimators and their estimates (often a source of confusion for students – especially in exams!) it moves on to definitions of classical properties of estimators: bias and efficiency and mean square error criteria including theoretical properties such as the Cramer-Rao bound for unbiased estimators. The chapter then looks at these properties via asymptotic notions of unbiasedness (consistency) and asymptotic efficiency. Interval estimation is included here as well with a very good discussion of coverage probabilities. Again many students still struggle to explain the frequentist notion of a confidence interval (sadly in exams again!) and the author does a good job of putting that right here as well as hinting of an alternative definition via the Bayesian paradigm. Finally, there is a short section providing a bridge to the latter chapters on hypothesis testing. The chapter concludes with an extended example of modelling cholesterol levels. I really liked this as it starts from postulating a statistical model, possible intuitive estimators of the mean and discussions of estimation, standard errors and confidence intervals. I especially liked the comparisons of the sample mean and sample median as competing estimators of the population mean. The author illustrates the relative efficiently via calculation and simulation which is very insightful. It was also nice to see a warning that one should always check the assumptions of your model (here the assumption of Normality) and actually under different assumptions the median may well be preferable. Students would gain a lot from the exercises in this chapter they contain a good deal of problems that develop intuition around the notions of efficiency.

Chapter 3 is a relatively short chapter introducing and discussing the properties of likelihood. After the usual definitions of the likelihood and log likelihood function for single parameter models are given and illustrated with examples there is a short section on sufficiency and its role in data reduction. The theory is a little deeper here with classical results such as the factorisation theorem and minimal sufficiency being given. …

… The author treads neatly around the philosophy of the likelihood principle directing the interested reader to other references for more foundational issues. Then it is back to practical matters such as dealing with multi-parameter models and the thorny issue of nuisance parameters mainly via the profile likelihood with pointers to the conditional, marginal and partial likelihood approaches. This is a bit of a shame as illustrating the conditional approach is normally something students at this level can grasp. If the content of the chapter is quite concise the principles are well illustrated in the end of chapter extended example (modelling stroke incidence). Here the practical issues of dealing with multi-parameter models and elimination of nuisance parameters are well described and the calculation shown in detail. Students would find this a useful way to link the material to the more realistic example.

Finally, in chapter 4 we move to estimation methods. As expected the chapter is centred around maximum likelihood estimation. The maximum likelihood estimator (MLE) is defined and some technical issues around properties of uniqueness are touched upon. However, like the previous chapters the focus is on practical issues of calculating the MLE (via elementary calculus in the one parameter case) and noting that numerical methods may be needed in more complex cases. Concepts of information are defined and asymptotic variance of the MLE is heuristically derived. Properties of the MLE are given (asymptotic unbiasedness and Normality, transformation invariance) and the delta-method for parameter transformations is derived. There are brief descriptions of the multi-parameter case and then alternative estimators (least squares, method of moments and via modified likelihoods). As usual the chapter ends with an extended example illustrating the material including obtaining confidence intervals. A nice touch is a discussion of how re-parameterising the problem may lead to a better Normal approximation in small samples.

Chapter 5 (like chapter 3) is a brief introduction to the classical elements of hypothesis testing. The first sections cover the definition of tests (point, one sided or two sided) and the definition of a statistical test and its constituent parts – hypothesis, test statistic, critical region and critical value. Given the recent and ongoing controversy over the use of statistical hypothesis tests in the literature I am pleased the author has a short section on acceptance versus non-rejection. Again many students (among others) fail to grasp this point. Types of statistical errors, power and sample size are then defined and illustrated. Finally, the author defines the most contentious issue the P-value (again an examiners nightmare!). After a careful technical definition, the author reminds readers of his previous warning and offers the advice that confidence intervals accompany any p-value. In future additions or assigned complimentary readings he might refer students to the recent American Statistical Association's statement on p-values and the associated discussions. The extended example is especially important here as it serves to reinforce the material and highlight the important issue sin interpretation.

Chapter 6 rounds out the material on classical inference dealing with specific types of hypothesis tests. The three standard test statistics (likelihood ratio, score and Wald tests) are defined and their asymptotic sampling distributions given. A brief section compares the advantages and disadvantages of each method. The extension to the multi-parameter case is given and a nice description of the various situations that arise in practice are given. A very brief section on inverting tests to obtain confidence intervals rounds out the essential material. The extended example in this chapter is the probably the most detailed and contains the most practicality of the other examples. This example is longer than the preceding theoretical discussion and relates the inferential principles to some very practical situations. I really liked the elements of "wisdom" expressed here and students will benefit from the translation of theory to practice.

Adding the Bayesian perspective in chapter 7 is to my mind a very useful counterweight to the preceding frequentist point of view. By necessity this is a very brief introduction to a huge subject. The level of mathematical and probability required is also at a higher level. The author does well to cover the basic philosophy and provide some intuition around the key ideas of the Bayesian approach. Illustrations are mainly through the use of conjugate priors as would be expected and I could not identify problems that involved applying computational solutions.

The final chapter addresses some special topics that could be best described under the umbrella of "non-parametric" or computational methods. Classical tests such as Fisher's exact tests, sign rank test and Wilcoxon-Mann-Whitney tests as shown and compared to the previous parametric approaches. The section on the Bootstrap and re-sampling methods is very brief and could only be described as a "taster" of this important topic.

The book is rounded off with appendices on properties of common distributions, the R code for the simulation examples used in the problems and a thoughtful collection of further reading.

So does this volume meet the criteria of "essential knowledge" as my MSc student would have it? I would say for the classical approach the book has an excellent coverage at about the right level for a well prepared MSc student. Stronger students may want more theoretical results and justifications which they would need to pursue via additional reading. I think the introduction to the Bayesian approach is well done albeit brief. I am less convinced by the very sparse space given to the Bootstrap and re-sampling methods and I think this is a place for expansion in a later addition to make it more self-contained for students.

Epilogue: Just as I finished this review I received my copy of the ISCB newsletter where this book was reviewed by Dr Miland Joshi. I agree with many of the points he raises (lack of diagrams, terse coverage of some areas and an informal approach to some important ideas) and I would concur that is would not be suitable for self-study. I am more positive and I would position it more as an enhanced set of lecture notes with the extended examples forming the basis of the student's work and the problems being the main focus in practical sessions. I feel that with some additions it could serve as foundation inference textbook in the more applied MSc programs.

David Collett	Modelling Survival Data in Medical Research (3rd ed.)	CRC	2014	9781439856789

This is a comprehensive text describing wide-ranging aspects of survival analysis in medical research: from the basic definitions and concepts to the regression methods and interpretation of results. In addition, advanced arguments such as frailty models, multiple events, and dependent censoring are treated. The book is illustrated by using many real-world examples of survival data in the medical field. Given the background and expertise of the author, the primary focus is on the use of survival analysis in clinical trials or observational clinical studies. It is well structured and easy to follow. Each chapter ends with a summary and detailed list of references. It is probably best suited to those with a quantitative background, but concepts are explained clearly and explicitly illustrated with examples. The level of detail is enough for a person wishing to have a general overview of survival analysis methods. Some chapters are more detailed than others, but the comprehensive lists of references provide plenty of information to direct the reader elsewhere if they require more depth.

The book contains 15 chapters, each of which is articulated in various sections and sub-sections. Briefly, the book can be divided in four parts. In the first part, from Chapter 1 to 4, the Author presents an introductory description of the basic survival concepts and estimators, and then introduces the well-known Cox proportional hazards regression model. This part also includes model checking techniques that are very useful in practical applications. Concepts introduced in this first part represent the basic ideas consequently used throughout the rest of the book. In this section the Author also explains the statistical inference underlying the described methods, the basic principles of estimation and useful strategies of regression modelling in practice (as for example methods to select covariates, definition of their functional form in the model, and comparisons among nested models). Part II presents parametric approaches to survival modelling, e.g. in Chapter 5 and 6 topics about parametric proportional hazards models, accelerated failure time and other less widely used methods, such as the proportional odds and the Royston and Parmar model, are discussed. This part is completed with model checking tools in parametric models exemplified in Chapter 7. Part III is constituted by four chapters, from 8 to 11, where a number of extensions to the basic models are presented. Time-dependent variables are introduced and discussed in the context of the Cox regression approach in Chapter 8; interval-censored data are treated in the framework of disease recurrences, in Chapter 9. Frailty (or random effects) models are presented in Chapter 10, with a detailed discussion about the different choices for frailty distributions and how to assess whether the unexplained variation observed in the data has been accounted for. Some methods to treat with the non-proportionality of the hazards is discussed in Chapter 11, with a specific reference to comparisons among data coming from different institutions. Several approaches are illustrated, as for example stratified models, piece-wise Cox regression, restricted mean survival estimation, pseudo-values, and the Poisson model to estimate the risk-adjusted failure rates. Finally, in Part IV, the general topic of multiple events is treated under different point of views: time to the first among multiple causes of failure, i.e. the competing risks methods, is introduced in Chapter 12. The reader will find here a clear and understandable discussion about the reason of failure of the standard methods in the competing risks setting and the need to formulate alternative approaches, such as the correct estimation of the cumulative incidence function and the Fine and Gray regression model. Chapter 13 is devoted to the "history modelling" approach for multiple events, i.e. when the interest lies in modelling transitions hazards among multiple events of the same type or a number of events of different types. Chapter 14 shows how dependent censoring can be taken into account when modelling survival data: basically, the inverse probability of censoring weights approach is presented, and the weighted version of the partial likelihood of the Cox regression model. Finally, Chapter 15 illustrates sample size requirements for a survival study, from the point of view of comparisons among treatments, which is a typical situation in a randomized clinical trial. Overall, the book is clearly written and well organized. It is easy to read and to comprehend the various conceptual and methodological issues related to survival analysis and its applicability to medical research. A useful integration would be to have also software references and some examples of typical codes (for example in R or Stata, the most commonly used ones) at the end of each chapter, in order to offer practical indications for the applied statistician. Moreover, a discussion about the predictive accuracy of the regression models in terms of calibration and discrimination is lacking and could be valuable to be included in a future edition. Finally, people working with large databases, e.g. health electronic administrative data, could benefit from a discussion devoted to possible extensions of survival methods able to deal with such big databases. In conclusion, this book represents a useful general reference to applied biostatisticians. By providing accessible coverage of the subject, it is an important source to acquire desired statistical skills regarding survival analysis, with a focus on applications of the methods and interpretation of the results. Further, it is equally helpful in scientific understanding of the most advanced research topics.

Book Review by Anna Bartkowiak (PL)

Gianluca Baio	Bayesian Methods in Health Economics	CRC	2012	9781439895559

The author is a distinguished specialist in Bayesian Methods applied in medicine, in particular in Health Economics. He is personally affiliated to two Universities (London and Milano Bicocca, where he held courses on "Statistical methods for Health Economics" and "Applied Health Economics". He participated in several projects where Bayesian analysis was essential for yielding a wide outlook. The book has grown out from the authors' research experience in that area. The book contains ca. 170 references to professional literature.

The reviewed book shows in a comprehensive way how Bayesian methods can be applied in various medical problems. This is done by formulating the proper statistical model ("a priori" probabilities) for data collected on purpose, and next to show how the model can be dealt with to yield interesting information in the form of distributions "a posteriori" and its statistics. The necessary software is discussed in detail.

The first chapter, written in collaboration with Rachel M. Hunter, is a general introduction to the principles of Health Economics and its major concepts. Among others, the concepts CMA (Cost Minimization Analysis), CBA (Cost Benefit Analysis), CEA (Cost Effectiveness Analysis), CUA (Cost Utility Analysis) are here discussed; also, how a health economic evaluation needs an integrated approach by methodologies of various different disciplines, like Epidemiology, Experimental Studies, Cost analysis, Decision theory, Causal inference, and so on.

Chapter 2 entitled "Introduction to Bayesian Inference" provides the mathematical and statistical foundations on the modelling and evaluating the Bayesian models. This is done considering four real examples:

(i) Diagnostic test T for a disease D with evaluating the inverse probability;

(ii) Inference on the probability of survival after a risky operation;

(iii) Estimating the proportion of female births in Paris in a certain time period;

(iv) Modelling the number of homicides per day in London.

According to the Bayesian philosophy, the probability assigned to any event depends on the individual whose uncertainty is being expressed on the background information that individual has available. Such an approach is called "subjectivist view". There is no assumption of a unique, correct ("true") value for the probability of any uncertain event. This is a completely different approach as the traditional (classic) one called the frequentist's approach. The author explains these approaches in detail and summarizes them in Table 2.2 ("The basic differences between the frequentist and the Bayesian approach"). The table considers the following items: nature of probability, nature of parameters, nature of inference, and interpretation of the phrases "We reject the hypothesis at the 5 percentage level of significance" (frequentist statement) and "The probability that this hypothesis is true is 0.05" (Bayesian statement). The frequentists construct 'confidence intervals', while the Bayesians evaluate 'credibility intervals'.

The key words and concepts considered (i.e. defined, explained and calculated) in this Chapter are: probabilities a priori, probabilities a posteriori, parametric modelling, predictive inference, credibility intervals, choosing prior distributions, Bayesian calculations (including vague priors, conjugate priors, Monte Carlo estimation, non-conjugate priors, Markov Chain Monte Carlo Methods (MCMC) with Gibbs sampling).

The lecture of the text is fascinating, yet it must be said that the lecture is not easy and a good background in mathematical statistics and probability theory is needed.

Chapter 3 is entitled "Statistical Cost-Effectiveness Analysis". In this Chapter the author returns to his true specialization: the health economics analyzed using the statistical approach. The presentations are illustrated by an Example on modelling the cost-effectiveness of a new Chemotherapy Drug. The statistical model with its distributional assumptions is formulated, and proper utility functions (like the net benefit) are defined. The author reviews here the main characteristics of decision theory. He assumes the standpoint that rational decision making is effected by maximizing the expectation of a suitable defined utility function. This is used to quantify the value associated with uncertain consequences of a possible intervention. The author links the general theoretical methodology to the specific problem. He specifies the problem in terms of composite response, accounting for both cost and benefits. He switches between the development of the theory and its application throughout. The author concentrates also on the development of sensitivity analysis techniques, which play a fundamental role in health economy evaluations. Continuing, some advanced issues like risk-aversion and the impact of market constraints, e.g. in the case of regulatory processes, are considered. All the analyses shown in the book can be obtained using the R package BCEA (Bayesian Cost-Effectiveness Analysis) written by the author (Baio, 2012) and downloadable from his homepage (www.statistica.it/gianluca/BMHE). The package needs access to a Bayesian MCMC sampler (like BUGS or JAGS, see Chapter 4).

Chapter 4, entitled "Bayesian analysis in practice", shows how the Bayesian issues can be calculated using appropriate software. The core of the computations is performed on samples (Gibbs samples) from the full conditional distributions. It happens in most practical situations, that the required conditional distributions are not analytically tractable and therefore it is necessary to approximate them, e.g. by Metropolis-Hastings or slice sampling algorithms. All this needs advanced programming which is implemented in the software called BUGS (Bayesian analysis Using Gibbs Sampling) and JAGS (Just Another Gibbs Sampler). Both software packages are free. BUGS has longer tradition. It is programmed in Component Pascal, a relative obscure language (phrasing of the author; myself, the reviewer, I would add the comment, that Pascal is truly no more in use).

Once compiled, BUGS works effectively and allows for semi-automatisation of the MCMC (Markov Chain Monte Carlo) sampling needed for specialist analysis. It has arguable contributed to the establishment of Bayesian statistics.

In recent years several programs have been written to interface the BUGS work with popular standard software like R, Matlab, Stata or SAS. JAGS is a relatively new (2010) and is programmed in C++. It makes approximately the same as BUGS, however it is easier to interface. Section 4 describes the main features of both packages and how to use them from within R. A detailed R scripts for analysis of the female birth data (total births = 493527, female births =246763) are presented. Also, detailed R scripts for elaboration of the chemotherapy drug example, considered already from theoretical point of view in Chapter 3, are shown now from computational point of view in section 4.7. One may find also in Chapter 4 interesting references, including many worked examples, with MCMC implemented either in the BUGS (or a variant of it) or the JAGS software.

Chapter 5 is entitled "Health economics evaluation in practice". The author focuses here on three particular cases: Case 1. Individual level data from a randomized controlled trial. A sample of patients is observed in relevant measures of cost and clinical outcome. Applying acupuncture for chronic headache in primary care was the treatment. Case 2. Neuraminidase inhibitors to reduce influenza in healthy adults. For each clinical scenario, the cost is determined by the use of the relevant resources. The probability of the outcome (influenza) varies with the intervention. Case 3. Markov model (MM) for the treatment of asthma, which allows the simulation of a follow up analysis on a "virtual" cohort of patients. All the examples are worked out starting from the description of the problem, the specification of the Bayesian model, and then presenting the code used to run the MCMC analysis and the post-processing necessary to derive the relevant health economics quantities used to produce the decision-making process.

The author maintains at his homepage (https://sites.google.com/a/statistica.it/gianluca/bookhe) a directory containing information on the content of the book and offering to read a sample for free. Additionally, one may find there, sources of data and codes (in R/JAGS) for the examples elaborated in the book. Also a list of typos and discussion of the book in the blog can be found there.

This is indeed a valuable supplement to the book. The book is nicely edited. The figures are well composed with easily readable text and axes labels. The text is composed in a transparent way with properly chosen fonts and spacing. It is a pleasure to take the book into one's hands and read the text.

The book is both theoretical at a high level, and very practical by presenting very detailed practical analyses - from the medical area - with computer code scripts. Due to the examples, which are understandable for anybody, I advise it to all kind of practitioners, not only from the medical area of applications.

Book Review (1) by Sada Nand Dwivedi (IN)

Chul Ahn, Moonseoung Heo, Song Zhang	Sample Size Calculations for Clustered and Longitudinal Outcomes in Clinical Research	CRC	2015	9781466556263

Under clinical research, one of the most common questions clinical biostatisticians encounter during interaction with collaborating investigators is “How many minimum number of subjects do I need to answer the research question (s) under this study?" For information of basically younger researchers, the required minimum sample size depends on a number of factors. For sample size calculation, obtaining such information is not trivial. It often involves literature review, preliminary studies, and sometimes even best guess. In the era of evidence based health care, the quality of evidence derived from a clinical research solely relies on how it is designed and executed. The calculation of required minimum sample size involving optimal level of confidence and power ensures that a study has adequate power to detect clinically meaningful effects more accurately. Such practice may sometime help in avoiding the risk of exposing excessive patients to experimental treatments caused by an overpowered study and also the waste in resources. However, studies involving correlated outcomes require more sophisticated methodologies for sample size calculation and analysis. As documented by the authors, experimental designs that generate correlated measurements of an outcome are widely used in biomedical, social, and behavioural studies. The correlated measurements are usually classified into two types: clustered or longitudinal.

In a clustered trial, randomization is performed at the level of some aggregate, such as schools, clinics, or communities. It is often adopted duo to necessity where the intervention under test is delivered on a group basis, for example, a radio campaign against smoking in a socially and economically disadvantaged community. On the other hand, in a longitudinal trial, randomization is performed at the individual level. However, over the study period the outcome variable is measured multiple times from the same individuals, hence giving rise to the issue of within-subject correlation. To clarify the difference between these two types of design, under the clustered design the measurements within a randomization unit (cluster) are usually considered exchangeable. Hence, the compound symmetric correlation structure needs to be frequently employed. However, under the longitudinal design, the measurements within a unit (individual) are distinguished by their time stamps due to the potential temporal trend. In this case, an autoregressive-type of correlation may be used more frequently which assumes the correlation to decay by the temporal distance between measurements. Further, correlated outcomes may also be encountered due to a hierarchical structure, which is even more complicated. For example, patients can be clustered by physicians, while physicians can be clustered by clinics. Thus, the correlation structure may contain multiple levels of nested clustering. As another example, patients may be clustered by physicians, but each patient contributes a longitudinal series of outcome measurements. In such cases, a hybrid type of correlation structure may be encountered. The premise throughout this book is sample size determination for clinical studies involving correlated outcomes. The authors conclude each chapter with a brief summary of covered contents along with related discussion and some recommendations for further readings and reference.

The present book encompasses six chapters, each of which is described under various sections with an attempt for better clarity to the readers. To introduce the principles under sample size considerations, the first chapter deals with basics of sample size calculation in case of independent outcomes. The authors have emphasized that sample size is usually estimated by precision analysis or power analysis. In precision analysis, sample size is determined by the standard error or the margin of error at a fixed significance level. Sample size estimation is needed for the study in which the goal is to estimate the unknown parameter with a certain degree of precision. In other words, the required confidence interval of a certain width, in which 100 % confidence level reflects the probability of including the true (but unknown) value of the parameter. Since the precision is determined by the width of the confidence interval, the goal of precision analysis is to determine the sample size that allows the confidence interval to be within a pre-specified width. The narrower confidence interval obviously indicates more precise estimate of the parameter. Further, confidence interval estimation provides a convenient alternative to significance testing in most situations. In power analysis, sample size is estimated to achieve a desired power for detecting a clinically or scientifically meaningful difference at a fixed level of significance. Power analysis is usually the most commonly used method for sample size estimation in clinical research. The sample size calculation requires assumptions that typically cannot be tested until the data have been collected from the trial. Sample size calculations are thus inherently hypothetical. The number of subjects in a clinical trial should always be optimal to provide a reliable answer to the questions being addressed. This number is usually determined by the primary objective of the trial. If the sample size is determined on some other basis, then this should be made clear and justified. Further, the primary endpoint should be chosen so that the primary objective of the trial can be assessed, and the primary endpoint is generally used for sample size estimation. The sample size calculation depends on the type of primary endpoint. The variable type of the primary outcome must be defined before sample size and power calculations can be conducted. The variable type may be continuous, categorical, ordinal, or survival. Categorical variables may have only two categories or more than two categories. Also, the primary purpose of a clinical trial is to address a scientific hypothesis, which is usually related to the evaluation of the efficacy and safety of a drug product. To address a hypothesis, different statistical methods are used depending on the type of question to be answered. Most often the hypothesis is related to compare the effectiveness of a new drug to that of a standard drug. Yet the specific comparison to be performed will depend on the hypothesis of interest. As an instance, for a superiority test, the necessary sample size depends on the clinically meaningful difference. An equivalence test is designed to confirm the absence of a meaningful difference between a standard drug and a new drug. The primary objective is to show that the mean responses to two drugs differ by an amount that is clinically unimportant. As claimed by the authors, they restrict the sample size estimation to a superiority test, which is most commonly used in clinical trials. In this chapter, they have reviewed sample size determination for independent outcomes. Hence, in their opinion, advanced readers who are already familiar with sample size problems can skip this chapter.

In second chapter, the authors have explored sample size determination for variants of clustered trials, including one-and two sample trials covering continuous and binary outcomes, stratified clustered randomization for binary outcomes, and nonparametric approaches for one-sample clustered binary outcomes. They have presented sample size formulas for varying cluster sizes using weighting schemes of equal weights to clusters, equal weight to observations, and minimum variance weights for one sample clustered outcomes. For two-sample clustered outcomes, they have listed sample size formulas for varying cluster sizes using equal weights to only observations. The most commonly used randomized cluster design is a parallel cluster randomized trial in which clusters are assigned to either an intervention or a non-intervention group in a random fashion. The advantages of a parallel design are simplicity and universal acceptance. The disadvantages are time and effort involved in their effective implementation, and large sample size for comparison, especially with low incidence outcomes. They have themselves opined that sample size formulas need to be developed using different weighing schemes such as equal weights to clusters and minimum variance weights for two sample clustered outcomes. In this chapter, they are restricted to only two-level data structures.

The authors have used a summary statistic approach for the estimation of sample size and power in repeated measurement studies in third chapter, since quite often the data for each subject may be effectively summarized by summary measures such as endpoint, difference score, or rate of change. Controlled clinical trials tend to employ a parallel-groups repeated measurement design in which study subjects are randomly assigned between treatment groups, evaluated at baseline and intervals across a treatment period of fixed duration. The repeated measurements are usually equally spaced, although not necessary so. The hypothesis of primary interest in short-term efficacy trials concerns the difference in patterns and magnitudes of change from baseline between treatment groups. Sample size estimate for repeated measurement studies is complicated since it involves specifying the missing data patterns, and the values of variance and correlation among the repeated measurements. Failing to specify appropriate variance and correlation patterns can lead to incorrect sample size estimates since the sample size estimate depends on the variances of each repeated measurements and the correlations among repeated measurements. Failure to include correlation between the repeated measurement outcomes can result in inappropriate sample size estimates and a more costly experiment. Missing data occurs more frequently due to missed visits in longitudinal studies than cross-sectional studies. Missing data may make it further difficult to write down the simple expression for the test statistic, and derive a sample size formula. As suggested by the authors, relative efficiency of summary measures approaches of endpoint analysis, difference score analysis, and rate of change analysis needs to be investigated for various correlation structures and missing data patterns.

…

A fundamental rule in sample size calculation is to align the model of sample size calculation with that of planned data analysis. The authors have correctly opined that sticking to this rule helps researchers avoid making type III error, which is, getting the right answer to a wrong problem. The two most popular approaches for regression analysis with correlated outcomes are the generalized estimation equation (GEE) and the mixed-effect models (MM). Both can be employed to analyze a wide variety of outcome variables, including continuous, binary, and count variables. The sample size approaches described in fourth chapter are appropriate for clinical trials where researchers have decided to analyze the data using the GEE method at the design stage for various types of correlated outcomes, including continuous, binary, and count. In this chapter, they have focused on the application of GEE sample size methods for clinical trials with only one level of correlation structure. The impact of missing data, correlation structures, and financial constraints is also investigated. The trade-off between the number of unique subjects and the number of measurements per subject can have profound implication in practice because the cost to recruit an additional subject and the cost to obtain an additional measurement from an existing subject usually differ dramatically. Achieving the optimal trade-off between these two designing parameters helps researchers improve the financial efficiency of clinical trials. They have further documented that difference in correlation structures alone explains why the sample sizes calculated based on the GEE and the MM methods might be different, even under the seemingly "equivalent" assumptions.

The sample size determination based on mixed-effects model approaches for randomized clinical trials with two level data structure has been presented in fifth chapter. They could explore longitudinal and cross-sectional factorial designs under balanced as well as unbalanced allocations. They have also compared them with sample size requirement in case of single level data structure. Under this, they could clearly demonstrate that trials with second level randomization require a large sample size compared to first level randomization. In addition, the authors have further extended the mixed-effects model sample size approaches described in fifth chapter to scenarios where three level data structures are involved in randomized trials (sixth chapter). Again, they have shown that for same values of other considerations, the sample size requirements are greatest for trials with the third level randomization, followed by second level randomization, followed by first level randomization. Further, they have also documented that the ratios of these sample sizes are identical regardless of whether the outcome is continuous or binary; one is testing main effects are interaction effects; or the designs are balanced or unbalanced. As a unique feature of the book, the authors have invariably provided further readings in the end of each chapter discussing not only different conditions but also providing relevant references dealing with sample size calculations in those conditions.

The authors have appropriately emphasized that sample size in clinical trials must be carefully estimated if the results are to be credible. If the number of subjects is too small, even a well-conducted trial will have little chance of detecting the hypothesized effect. Ideally, the sample size should be optimally large to have a high probability of detecting a clinically important difference between treatment groups and to show it to be statistically significant if such a difference really exists. But, if the number of subjects is too large, the clinical trial will lead to statistical significance for an effect of little clinical importance. Conversely the clinical trial may not lead to statistical significance despite a large difference that is clinically important if the number of subjects is too small. When an investigator designs a study, an investigator should consider constraints such as time, cost, and the number of available subjects. However, these constraints should not dictate the sample size. The authors have further emphasized that there is no reason to carry out a study that is too small, only to come up with results that are inconclusive. Under such cases, investigator will need to carry out another study to confirm or refute the initial results. To summarize, choosing an appropriate sample size increases the chance of detecting a clinically meaningful effect and ensures that the study is both ethical and cost-effective. Hence, selecting an appropriate sample size is a crucial step in the design of a clinical study.

In summary, this is a clearly written and sequentially well organized book. One may find it easy to read and comprehend the various conceptual and methodological issues. To facilitate better understanding, each of the covered topic deals with illustration. The authors, while jointly addressing the over-arching theme of sample size determination for correlated outcome under such settings, have written individual chapters in a self-contained manner so that readers can explore specific topics relevant to their research projects without having to refer to other chapters. I fully agree with the claim of the authors that this book may serve as a useful resource for biostatisticians, clinical investigators, epidemiologists, and social scientists whose research involves randomized trials with correlated outcomes usually classified into two types: clustered or longitudinal. Further, it may be equally helpful in scientific understanding of related research articles and their critical appraisal.

Book Review (2) by Sada Nand Dwivedi (IN)

Alessandro Baldi Antognini, Alessandra Giovagnoli	Adaptive Designs for Sequential Treatment Allocation	CRC	2015	9781466505759

The evidence based health care is equally desired even in the area of clinical practice involving serious prognosis, side effects and outcomes. In such areas, use of sequential treatment allocation becomes unavoidable. This book has genuinely addressed the issue of designing experiments for comparing two or more treatments, when the experiment is sequential. This type of experimental design is called adaptive once the investigator wishes to make use of the information accrued along the way. The authors have reviewed and reorganized the existing results of adaptive design theory with focus to its mathematical foundation. As a research book, keeping in view of available computer facilities, their approach is essentially theoretical, highlighting the mathematical difficulties and the statistical properties of adaptive designs as regards statistical inference following the experiment. As pointed out by the authors, this book may complement part of the present day literature in which a large number of authors base their conclusions on simulations. As reported by them, simulations are generally very useful, but not always sufficiently convincing, and in some cases they may be plainly misleading. Further, they have addressed the issues in general, not to a particular application. To be more specific, it is not a book on clinical trials, although a large number of the designs they present are clearly inspired by clinical and pharmaceutical research, and the vast bibliography dedicated to this field.

The statistical models most commonly used in comparative experiments are introduced in first chapter. The authors have presented target allocations of the treatments motivated by inferential considerations, and given new conditions for the convergence of a sequential experiment to a given target. A discussion of asymptotic inference plays a central role in this chapter. A unifying definition (Markovian Designs) has also been introduced by them to describe a large class of adaptive designs that share interesting properties. They have further emphasized the role of randomization throughout, as an important tool to avoid several types of bias. The randomized adaptive designs that they have presented in the remaining chapters are grouped mainly according to methods of construction.

The second chapter has illustrated designs whose assignment rules take into account past treatment allocations only. This chapter is about adaptive random allocation rules which depend on the past history of the experiment only through the sequence of previous treatment assignments. Such allocation rules have the advantage that the whole experiment can be designed in advance, before collecting the responses, and inference may be conditional on the design. As another important issue, in a large number of comparative experiments, the researchers would like to achieve a balanced or near balanced allocation among the treatments. …

Balance is often related to inferential optimality. However, it is fairly intuitive that balance and randomness are conflicting demands. The major focus of the present chapter is allocation-adaptive designs intended to achieve some balance and maintain a good degree of randomness in the assignments. The requirement of a suitable trade-off between inferential optimality and unpredictability is particularly cogent for Phase III trials. Under this phase of trial, patients are enrolled sequentially and the total sample size is often a priori unknown, so that keeping a reasonable degree of balance at each step, while maintaining a good degree of overall randomness, could be crucial to allow the experiment to be stopped at any time in a good inferential setting. In order to compare different designs, the need has arisen to find ways of measuring the degree of randomness and the degree of imbalance of an allocation rule. The indicators of imbalance and predictability suggested in the literature are also described in this chapter.

In contrary to described adaptive allocation methods based on previous treatment allocations in second chapter, sometimes it is intuitively very appealing to choose progressive assignments on the basis of the observed outcomes as well. The randomization procedures that depend on the responses might sometime be a necessity. For instance, ethical concerns about the risks for the subjects involved in the trial, or to economic concern for costs. Hence, in third chapter, the authors have dealt with those designs that also make use of past data, like sequential maximum likelihood designs and doubly-adaptive designs, with a further section on the topic of up-and-down experiments. Instead of the comparisons between various qualitative treatments, the underlying framework may be a set of ordered treatments, like doses of a given drug that might be toxic. The Up-and-Down are a class of response-adaptive designs aimed at finding which among treatment levels will produce a desirable pre-specified expected response. Although this algorithm was originally introduced for binary outcomes, they have also discussed a version that can be applied for any real response variable.

After presenting adaptive designs according to the construction methods of the randomization mechanism in previous two chapters, the authors have taken into account of the motivations in forth chapter, usually of an ethical nature, that lie beneath a vast class of adaptive designs. There are different ways of evaluating the usefulness of an experiment. One type of utility, the type they have been dealing with in earlier chapters, is related to the information collected from the experiment, measured in terms of design optimality criteria. Another type is related to the output, for instance one might define the utility of an experiment in terms of the total expected outcome. Some experiments are multipurpose, aimed at improving the expected returns as well as gathering information for inference about the treatments. In fourth chapter, the authors have dealt with multipurpose adaptive experiments involving step by step procedures. To be more specific, in a clinical trial for comparing two or more treatments, the experimenter may have both goals in mind: (i) determining which, if any, is the superior treatment and how much better it is than the competitors; and (ii) favouring the allocation of patients to the treatment that appears to be superior as evidence about the treatment effects is gathered during the experiment. As obvious, the first is an inferential goal that reflects a possible benefit for future subjects; the second expresses an ethical responsibility to current subjects in the study. In order to achieve first goal efficiently, second goal may have to be sacrificed, and vice versa. In their words, this dilemma is described as "individual versus collective ethics". Due to its importance, this problem is often addressed in wide variety of disciplines, such as engineering, game theory, control theory, operational research, information theory, simulation-based optimization, genetic algorithms, reinforcement learning, as well as clinical research.

The fifth chapter deals with multipurpose adaptive designs involving constrained and combined optimality that achieve a good trade-off between different experimental goals. In contrary to fourth chapter, at each step the allocation probability is the result of a compromise between inferential optimality and randomness and/or ethical demands. In this chapter, they have started from design criteria that formalize the experimental objectives and find targets that are optimal with respect to some compromise of the criteria. Within this context, two different approaches are possible, (i) constrained target that is derived by optimizing a given criterion under suitable constraints on the other criteria; and (ii) combined optimization target that optimizes a suitably chosen compound criterion that combines the different experimental goals by means of suitable weights. In general, the optimal target allocations derived through these approaches depend on the unknown model parameters and therefore suitable response-adaptive procedures, such as those described in third chapter, must be called for in order to converge to them. In other words, the acquisition of covariate information (like prognostic factors, biomarkers) about the statistical units involved in the experiment is also of fundamental importance and should not be ignored in the design.

In sixth chapter, the authors have revisited adaptive experiments to include covariates and new adaptive methods for this context. Real life experiments, especially clinical trials, usually involve additional information on the experimental units, in the form of a set of covariates, e.g. important prognostic factors for patients. As reported by the authors, taking these covariates into account is of primary importance for a correct inference, and it must be a fundamental concern from a design perspective in sequential experiments as well. The literature on adaptive randomization has been focusing the attention on this issue. The authors have discussed the importance of balanced designs under the assumptions of linear homo-scedastic model incorporating covariates. Further, they have discussed the sequential methods that adapt for covariates regardless of the responses, namely minimization, the procedures based on Optimal Design theory and the stratified randomization mechanisms formalized in the general class of Covariate-adaptive designs. They have also addressed compound optimal designs that combine efficiency with ethical or economical gain making use of the covariates. They have further mentioned some suggestions of designs for models with covariates other than the linear homo-scedastic one.

Throughout this book, the authors have made extensive reference to design optimality in the context of adaptive experiments, and the basic tools of optimal design theory used in this book are included as a separate appendix. Although their approach is frequentist, they have also included another appendix on Bayesian adaptive designs that are conceptually very important. They have themselves accepted that several issues of great relevance for applied adaptive designs are not included or not fully discussed in this book, such as dose-ranging estimation, sample size re-estimation, adaptive hypotheses designs and seamless trial designs, to mention just a few. They have opined that the theoretic study of some of these methodologies has not reached sufficient maturity to be included in this book. Some other central topics are just hinted at, the most prominent of which is stopping rules (at the end of Chapter 1). They have reported that there already exist outstanding books on this subject. Further. as accepted by the authors, because of involvement of a model-based approach in this book, they did not include designing experiments for randomization-based inference.

In summary, the readers of this book need to have fair knowledge of elementary algebra, calculus and probability, and rudimentary notions of stochastic processes especially the theory of Markov chains. Although the authors have tried to avoid making explicit use of more advanced mathematical tools, such as Martingale theory, some of the results they present (without proofs) are indeed based on such theories. I fully endorse views of the authors that researchers working in the area of adaptive designs may find this book a useful reference. Further, since this book includes a fair number of examples, teachers of graduate-level courses on designs may also find this book useful.

Jialiang Li, Shuangge Ma	Survival Analysis in Medicine and Genetics	CRC	2013	9781439893111

This book cannot be considered a simple introduction to survival analysis techniques. On the contrary, the authors have selected three advanced topics of interest for the analysis of medical or genomics data: analysis of interval censored data, diagnostics tests and analysis of high dimensional data. Additional chapters cover in less detail both introductory concepts and special modelling methods such as multivariate survival models, competing risk analysis and cure rate models.

The emphasis of the authors is to provide a rigorous approach to the analytical techniques described, more than an intuitive or practical approach. The book will be valuable for graduate students in biostatistics aiming to have a comprehensive coverage of these topics. Though the techniques are motivated with good examples, introduced in chapter 1, and software to perform the analysis are mentioned at the end of each section, the focus of the book is essentially theoretical. This emphasis is clear from the preface. Those interested in detailed tutorials on analysis are addressed to other texts. All the topics covered are very well cited, and most references are relatively recent.

I found the title of the book misleading, since there is nothing specific to the analysis of genetic data, in the sense of methods to study inheritance. There are some examples that refer to somatic mutations as genetic data, and the last chapter mentions genetic association studies as an example with multidimensional data, but most examples correspond to genomics. I was expecting a section covering the analysis of haplotypes with survival data, but there is nothing specific to genetics. Other than that, the book is an excellent review of techniques useful for the analysis of time to event data in medicine.

Classical approaches of survival analysis in the simplest scenario of right censoring are covered in chapter 2. It is comprehensive, but I found this chapter advanced and not useful as introductory to the topic for someone without previous knowledge on survival analysis. The aim of the chapter is more a review of the concepts, serving as starting point for later chapters and setting of notation.

I found chapter 3 the best one of the book. It covers interval censored data in great detail, including the theoretical elements that support the proposed methods of analysis. Two types of interval censored data are introduced: in type I the event of interest is known to have occurred before some censoring time, but the exact time is unknown. In type II, the event is known to have occurred in a bounded interval before a censoring time, but after a previous time. Parametric, non-parametric and semi-parametric approaches to the estimation of the survival function are explained, followed by methods to compare survival functions. Their properties are justified in detail. This chapter is excellent for students or practicing statisticians in need of a well justified theory of the state of the art methods for interval censored data. Some examples are used throughout the chapter, however, readers with need of a more intuitive and practical approach are referred to the book by J. Sun (Springer 2006).

Chapter 4 combines diverse topics in a compact and advanced approach, similar to the introductory chapter 2. I found that the coverage of multivariate models for the analysis of correlated data, competing risk models and cure rate models was correct, but in a low degree of detail, without examples. These topics are very relevant in practice, but the authors opted to cover them in a summarized version. The chapter also includes a section on nonparametric analysis of covariates and Bayesian approaches to analyse complex survival models. Though the authors declare themselves frequentists, they acknowledge the value of Bayesian methods in the field.

Chapter 5 is a rigorous and complete coverage of the theory to analyse diagnostic tests. The initial sections cover the analysis of a binary and continuous diagnostic test. The measures of diagnostic accuracy are described and their distribution properties derived, both under parametric and nonparametric approaches. The analysis of multiple predictors is also introduced, and measures of incremental predictive accuracy. The last sections are devoted to the extension of the accuracy measures to survival data, under different censoring situations. The analysis of right censored data is well covered. Though most of the material of this chapter is not related to survival data, it is a great review of the analysis of diagnostic tests and worth reading for anyone working in the analysis of diagnostic and prognostic biomarkers.

The last chapter, 6, includes a survey of methods useful for the analysis of high dimensional data, as usually arises in genomics. Methods to control for multiple testing are explained when the analysis of interest is the marginal association of each variable. These methods (Bonferroni correction and false discovery rates) are not specific to survival analysis. The second section in this chapter deals with methods to reduce dimensionality. Three approaches to apply partial least squares with censored data are suggested, but not detailed, since there is no theoretical justification yet. Principal components analysis to reduce covariates is explained in detail, but this technique is not unique to survival data. Methods for variable selection are also explained in detail, first those based on step-wise model building, that depend on measures of goodness of fit, and second methods based on penalised likelihood estimation like lasso, elastic nets, bridge penalty, smoothly clipped absolute deviation (SCAD) penalty and minimax concave penalty (MCP).

In summary, this book contains an excellent theoretical coverage of interval censored data, and deals with other topics relevant for survival analysis in a comprehensive but summarized way.

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President, **KyungMann Kim**	Educ	Department of Biostatistics and Medical Informatics, University of Wisconsin School of Medicine and Public Health, 600 Highland Ave, K6/438 CSC, Madison, WI 57392-4675, USA	+1 608 265 6380	kyungmann.kim@wisc.edu

Professor of Biostatistics and Statistics, University of Wisconsin-Madison. His current area of research includes sequential analysis, cluster data analysis and clinical and translation research in cancer, cardiovascular disease, obesity and gerontology. He is very active in professional services to the US National Institutes of Health (NIH) and as data monitoring committee member on many NIH- and industry-sponsored clinical trials in various diseases.

He has been a member of the Society since 1998. He served as an elected member of the ISCB Executive Committee during 2006-2010 and as a member and chair of the Student Conference Award Subcommittee during 2006-2010 and a member of the Membership Subcommittee during 2007-2010. Served as ISCB Treasurer from 2011-14.

Vice-President: **Vana Sypsa**	Epid	Department of Hygiene, Epidemiology and Medical Statistics, Athens University Medical School, M. Asias 75, 11527, Athens, Greece	+30 210 7462193	vsipsa@med.uoa.gr

Assistant Professor of Epidemiology and Preventive Medicine at the Department of Hygiene, Epidemiology and Medical Statistics of the University of Athens (Greece). My current areas of research include infectious diseases epidemiology and mathematical modeling as well as interventions to prevent HIV and viral hepatitis.

I participated actively in the organisation of the annual ISCB conference in Alexandroupolis, Greece (2007). I served as member of the Student Conference Awards Subcommittee (2005-2011) and as Chair and member of the Epidemiology Subcommittee (2009-2012 and 2012-today, respectively). I served as an elected member of the ISCB Executive Committee from 2005-2008 and as Secretary of the Society from 2013-2016.

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Zdenek works as research fellow at the Department of Medical Informatics & Biostatistics of the Institute of Computer Science, Czech Academy of Sciences in Prague. He also teaches a course in Survival Analysis at the Faculty of Science of the Masaryk University in Brno. His research interests include survival analysis and statistical modelling in general, also involving high-dimensional data. Zdenek also holds an appointment with the Czech Science Foundation for reviewing grant proposals (2015-18).

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Secretary: **Geir Egil Eide**	Conf	Centre for Clinical Research, Haukeland University Hospital, N-5021 Bergen, Norway	+47 97559734	geir.egil.eide@helse-bergen.no

Geir Egil Eide has since 1999 been Biostatistician at the Centre for Clinical Research, Haukeland University Hospital, Bergen, Norway and is Adjunct Professor of Clinical Biostatistics at the Department of Global Public Health and Primary Care, University of Bergen (UoB). He received his MSc (CandReal) in Mathematical Statistics in 1977 from the UoB, and PhD (DrPhilos) in 2008 with a thesis on attributable fractions. He has collaborated closely with medical and health related researchers since 1979. He has extensive teaching experience and teaches medical students in statistics and epidemiological methods.

He has been a member of the Subcommittee on Epidemiology since its formation. He chaired the Local Organising Committee for the ISCB conference in Bergen in 2012, and is a member of the Conference Organising Subcommittee (chair from 2017).

Who	SCs	Address	Tel:	Email:
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Hein Putter	NatG, StCA	Department of Medical Statistics and Bioinformatics, Leiden University Medical Center, Postzone S-5-P, PO Box 9600, 2300 RC, Leiden, Netherlands	+31 71 5269705	h.putter@lumc.nl
Katherine Lee	Conf, StCa	Murdoch Children's Research Institute, Royal Children's Hospital, Flemington Road, Melbourne, VIC 3185, Australia	+61 3 934565	katherine.lee@mcri.edu.au
Nadine Binder	StCA	Institute for Medical Biometry and Statistics, Medical Center-University of Freiburg, Stefan-Meier-Str. 26, 79104 Freiburg, Germany	+49 761 2036662	nadine.binder@imbi.uni-freiburg.de
Stanislav Katina	NatG, SiRA	Institute of Mathematics and Statistics, Faculty of Science, Masaryk University, Kotlářská 267/2, 611 37 Brno, Czech Republic	+420 549 49 7265	111465@mail.muni.cz
Thomas Jaki	Educ, StCA	Department of Mathematics and Statistics, Lancaster University, Lancaster LA1 4YF, UK	+44 1524 592318	jaki.thomas@gmail.com
Tomasz Burzykowski	Conf, NatG	I-BioStat, Hasselt University, Agoralaan D, 3590 Diepenbeek, Belgium	+32 11 268243	tomasz.burzykowski@uhasselt.be
Toshiro Tango	Conf	Center for Medical Statistics, SAN Bldg. 4F 2-9-6 Higashi Shimbashi, Minato-ku Tokyo 105-0021, Japan	+81 3 6450 1680	tango@medstat.jp

ISCB Membership and Googlegroups Emailing Lists

From Rita Schou (ISCB Office) and David W. Warne (Googlegroup Administrator)

We try to make sure our membership database (in Denmark) is kept up to date.

We also have an electronic mailing list called iscb@googlegroups.com, which allows members from the current and past years to be contacted to discuss statistical ideas and to receive news about ISCB events.

From time to time we compare the 2 databases and if we find you've got 2 email addresses, we'll ask which you prefer.

If you haven't done so already, please send us your email address to allow us to contact you more easily.

If you've sent us your email, but haven't accepted the invitation to join the ISCB googlegroup, please accept the next invitation by pressing Reply-Send.

Rest assured that no company will send you any junk email – all emails are checked by the Office or the Googlegroup Administrator.

ISCB Subcommittees: Contact Details

Please contact the chairs/secretaries of these subcommittees for further information.

Title & Email	Terms of Reference	Members	Email addresses
Conference Organising iscb-conf-org@ googlegroups.com	1. Bring together ISCB conference organisers or ISCB members who have an interest in sharing and passing on their knowledge and experience to help future ISCB conference organisers. 2. Document processes and systems for assisting ISCB conference organisers. 3. Review and update the documents whenever necessary and promote their usage for improving the procedures or conferences.	Chair:	
		1. Geir Egil Eide (NO)	geir.egil.eide@helse-bergen.no
		Secretary:	
		2. Jörg Assmus (NO)	assmus@uni.no
		Members:	
		3. David W. Warne (CH)	david_w_warne@bluewin.ch
		4. Jacobo de Una Alvarez (ES)	jacobo@uvigo.es
		5. Katherine Lee (AU)	katherine.lee@mcri.edu.au
		6. Koos Zwinderman (NL)	a.h.zwinderman@amc.uva.nl
		7. Lucinda Billingham (UK)	L.J.Billingham@bham.ac.uk
		8. Maarten Schipper (NL)	maarten.schipper@rivm.nl
		9. Michael Schemper (AT)	michael.schemper@meduniwien.ac.at
		10. Tim Ramsay (CA)	tramsay@ohri.ca
		11. Tomasz Burzykowski (BE)	tomasz.burzykowski@uhasselt.be
		12. Toshiro Tango (JP)	tango@medstat.jp
		13. Ulrich Mansmann (DE)	mansmann@ibe.med.uni-muenchen.de
		14. Zdenek Valenta (CZ)	zdenek.valenta@me.com
Education iscb-education@ googlegroups.com	To support and organise educational activities, such as short-courses, webinars and seminars on contemporary methods in clinical biostatistics. Guidelines and a list of activities in the past are available.	Chair:	
		1. Erik Cobo (ES)	erik.cobo@upc.edu
		Secretary:	
		2. Thomas Jaki (UK)	jaki.thomas@gmail.com
		Members:	
		3. Alexia Iasonos (US)	iasonosa@mskcc.org
		4. Anca Vitcu (RO)	avitcu@yahoo.com
		5. Catherine Quantin (FR)	catherine.quantin@chu-dijon.fr
		6. Dawn Teare (UK)	m.d.teare@sheffield.ac.uk
		7. Jeremy Taylor (US)	jmgt@umich.edu
		8. KyungMann Kim (US)	kyungmann.kim@wisc.edu
		9. Rumana Omar (UK)	r.omar@ucl.ac.uk
		10. Shona Fielding (UK)	s.fielding@abdn.ac.uk
Epidemiology iscb-epidemiology@ googlegroups.com	1. Advise the Scientific Programme Committee of the annual ISCB meetings, if needed, on relevant topics in epidemiology for establishing invited sessions and choosing invited speakers. 2. Establish connections with Epidemiological Societies and organise mutual sessions, courses or workshops at our conferences or elsewhere. 3. Generate awareness and discussions in the Society of guidelines for conducting, analysing and reporting epidemiological studies.	Chair:	
		1. Saskia Le Cessie (NL)	S.le_Cessie@lumc.nl
		Secretary:	
		2. Christina Bamia (GR)	cbamia@nut.uoa.gr
		Members:	
		3. Agus Salim (AU)	A.Salim@latrobe.edu.au
		4. Catherine Quantin (FR)	catherine.quantin@chu-dijon.fr
		5. Ewout Steyerberg (NL)	E.Steyerberg@erasmusmc.nl
		6. Harbajan Chadha-Boreham (FR)	harbajan.kcb@gmail.com
		7. Nathalie Stoer (SE)	nathalie.stoer@ki.se
		8. Tim Ramsay (CA)	tramsay@ohri.ca
		9. Vana Sypsa (GR)	vsipsa@med.uoa.gr
		10. Willi Sauerbrei (DE)	wfs@imbi.uni-freiburg.de

Title & Email	Terms of Reference	Members	Email addresses
National Groups iscb-national-groups@googlegroups.com	1. To help those interested in forming a National Group through the approval process as described in the Constitution. 2. To review the arrangements with the current National Groups. 3. To set rules and standards for funding of ISCB members of National Groups. 4. The Subcommittee administers the Conference Awards for Scientists for the annual ISCB meetings.	Chair:	
		1. Zdenek Valenta (CZ)	zdenek.valenta@me.com
		Secretary:	
		2. Anca Vitcu (RO)	avitcu@yahoo.com
		Members:	
		3. Chris Metcalfe (UK)	chris.metcalfe@bristol.ac.uk
		4. David W. Warne (CH)	david_w_warne@bluewin.ch
		5. Gordana Jovic (UK)	g.jovic@ucl.ac.uk
		6. Hein Putter (NL)	h.putter@lumc.nl
		7. Kinga Salapa (PL)	kinga.salapa@uj.edu.pl
		8. Laszlo Tothfalusi (HU)	tothfalusi.laszlo@pharma.semmelweis-univ.hu
		9. Stanislav Katina (CZ)	111465@mail.muni.cz
		10. Tomasz Burzykowski (BE)	tomasz.burzykowski@uhasselt.be
		11. Zsolt Lang (HU)	Lang.Zsolt@univet.hu
Statistics in Regulatory Affairs iscb-reg-aff@googlegroups.com	The subcommittee on Regulatory Affairs will review, comment upon and seek to influence the development of regulatory requirements, guidelines and other documents concerning the scientific aspects of data generation, collection, management, analysis, and reporting. In general, the subcommittee will seek out and handle all regulatory issues in the name of the Society with the approval of the President or in his/her absence, the Vice-President.	Chair:	
		1. Harbajan Chadha-Boreham (FR)	harbajan.kcb@gmail.com
		Secretary:	
		2. Nicole Close (US)	nclose@empiristat.com
		Members:	
		3. Chris Weir (UK)	christopher.weir@ed.ac.uk
		4. Christoph Gerlinger (DE)	christoph.gerlinger@bayer.com
		5. Christos Nakas (GR)	cnakas@gmail.com
		6. Jonathan Siegel (US)	jonathan.siegel@bayer.com
		7. Jørgen Seldrup (FR)	Jorgen.seldrup@quintiles.com
		8. Juan Vicente Torres-Martin (ES)	jvtorres@syntaxfs.com
		9. Martin Schumacher (DE)	ms@imbi.uni-freiburg.de
		10. Ralf Bender (DE)	Ralf.Bender@iqwig.de
		11. Stanislav Katina (CZ)	111465@mail.muni.cz
		12. Tim Friede (DE)	tim.friede@med.uni-goettingen.de
Student Conference Awards iscb-stud-conf-awrd@googlegroups.com	Student conference awards are available for registered postgraduate students to attend the annual conference and present a paper. The Subcommittee shall receive submissions, judge them, and administer the awards. The rules and procedures are announced in a timely issue of the Newsletter and on the ISCB annual conference webpage.	Chair:	
		1. Nadine Binder (DE)	nadine.binder@imbi.uni-freiburg.de
		Secretary:	
		2. Katherine Lee (AU)	katherine.lee@mcri.edu.au
		Members:	
		3. Carl-Fredrik Burman (SE)	carl-fredrik.burman@astrazeneca.com
		4. Chris Metcalfe (UK)	chris.metcalfe@bristol.ac.uk
		5. Dimitris Rizopoulos (NL)	d.rizopoulos@erasmusmc.nl
		6. Hein Putter (NL)	h.putter@lumc.nl
		7. Jeremy Taylor (US)	jmgt@umich.edu
		8. Richard Cook (CA)	rjcook@uwaterloo.ca
		9. Thomas Jaki (UK)	jaki.thomas@gmail.com
		10. Ulrich Mansmann (DE)	mansmann@ibe.med.uni-muenchen.de

The International Society for Clinical Biostatistics (ISCB) was founded in 1978 to stimulate research into the principles and methodology used in the design and analysis of clinical research and to increase the relevance of statistical theory to the real world of clinical medicine.

The ISCB organises an annual scientific meeting which members and non-members are able to attend. The main objective of the annual scientific meetings is to create an opportunity for the exchange of knowledge, experience and ideas among clinicians, statisticians and members of other disciplines, such as epidemiologists, clinical chemists and clinical pharmacologists, working or interested in, the field of clinical biostatistics.

The scientific meetings cover a broad spectrum of biostatistical interests and regularly include sessions on the design and analysis of clinical trials, epidemiology and statistical methodology, as well as from time to time considering more specialist issues such as, for example, education of biometricians and biometrics users, pharmacokinetics, medical databases and pharmaco-epidemiology.

Meetings in recent years have been held in Alexandroupolis (2007), Copenhagen (2008), Prague (2009), Montpellier (2010), Ottawa (2011), Bergen (2012), Munich (2013), Vienna (2014), Utrecht (2015) and Birmingham (2016). The next meetings will be held in Vigo (2017), Melbourne (2018), Leuven (2019) and Krakow (2020).

The Annual General Meeting of the ISCB is organised to coincide with the scientific meeting. Membership of the Society is drawn from around 50 countries worldwide and the number of members is about 1030.

The ISCB also organises courses to cover particular statistical topics and are given by the foremost researchers in the field. These are run to precede or follow on from the annual scientific meeting, or are run as separate events.

The composition of the Executive Committee (ExCom) for 2017 is as follows:

Officers	
President	KyungMann Kim (US)
Vice-President	Vana Sypsa (GR)
Treasurer	Zdenek Valenta (CZ)
Secretary	Geir Egil Eide (NO)

Members	
Chris Weir (UK)	Stanislav Katina (CZ)
Hein Putter (NL)	Thomas Jaki (UK)
Katherine Lee (AU)	Tomasz Burzykowski (BE)
Nadine Binder (DE)	Toshiro Tango (JP)
Past President,	David W. Warne (CH)
News Editor, Webmaster	

The ISCB also has special Subcommittees dealing with particular aspects of biostatistics.

The Society publishes a Newsletter twice a year. The ISCB News editor is David W. Warne. Items for inclusion in the Newsletter should be sent to him via email to: david_w_warne@bluewin.ch

Membership of the Society is open to all with an interest in biostatistics. The current annual (to 31 December 2017) Ordinary membership fee is €40. The Full-time Student and Retired Membership fee is €10. There are reduced fees for members (€20) and students (€5) from Developing Countries, as defined by the World Bank list. All who subscribe after April will have to pay an extra fee of €20.

Applications for membership should be sent by email to:

ISCB Permanent Office Bregnerodvej 132, DK-3460 Birkerod, Denmark	Tel: +45 2682 7970 email: office@iscb.info www: www.iscb.info

INTERNATIONAL SOCIETY FOR CLINICAL BIOSTATISTICS
2017 Membership Subscription

Surname:		First name:	
Title (Prof/Dr/etc):		Post held:	
Institute/Company:			
Address:			
Post code and country:			
Phone No.:		E-mail:	
Fax No.:		**Please provide your email address in order to log on to the Members' Area of ISCB's website; it may be used to send you the electronic ISCB News in the future, and is needed for voting.**	
Member No.:			

	Registration Jan.-Apr.	Late registration May-Dec.	ISCB membership to 31 December 2017:	
SUBSCRIPTION:	❑ EUR 40	❑ EUR 60	Regular members	
(please tick one only)	❑ EUR 10	❑ EUR 30	Student Member (applicable to undergraduate or postgraduate -Masters or PhD- students) (students should provide a letter from their supervisor or head of department)	
	❑ EUR 10	❑ EUR 30	Retired members	
	❑ EUR 20	❑ EUR 40	DC members	Developing Country
	❑ EUR 5	❑ EUR 25	DC student members	Developing Country
Have you previously been a member of ISCB?	❑ Yes	❑ No		

New members: Please send this Membership Subscription form to office@iscb.info.
Your details will be uploaded to the Members' Area of ISCB's website,
and you will be notified when you can follow the procedure below.
Current members: Please log on to the Members' Area with your e-mail address.

PAYMENT IS MADE BY: ❑ **On-line**

- Go to http://www.iscb.info/Members-Area.html
- Apply for your password by clicking on "forgotten password"
- Type your email address and click on "Send password" You receive your password by email

- Log on to the **Members' Area** using your e-mail address and your password.
- Click **Renew membership** on the left-hand bar –
  accept conditions – accept order – select payment method – Maestro / Master Card / Visa / Visa Electron / JCB - and complete payment. You will receive an email from us confirming that you have renewed your membership once your payment is completed.

Your address details and membership category are already entered into the system. In the **Members' Area** you can edit your **Profile Settings**, except your e-mail address. Please contact office@iscb.info if you wish to change your e-mail address.

Please note that ISCB's online payment facility is a secured system; your credit card information cannot be accessed or used for any other purpose.

PS: Danish VISA/Dankort cards are not supported.
If you wish to pay your membership fee by bank transfer we ask you kindly to contact the Permanent Office for ISCB's bank account details (office@iscb.info).

Please return this form either by e-mail to: office@iscb.info
or by post to: ISCB Permanent Office
Bregnerodvej 132
DK-3460 Birkerod
Denmark
Tel: +45 2682 7970

ISCB is affiliated to ISI. For the latest conference information, see:
http://www.isi-web.org/index.php/activities/calendar

2017: 23-25 Jan	*Young European Statistician (YES VIII) meeting* The next edition of Young European Statistician (YES VIII) meeting will be held on the 23-25 of Jan, 2017, at Eurandom, Eindhoven. This year the workshop aims to bring together young researchers (PhD students, postdocs and young faculty members) working (or interested) in the field of uncertainty quantification (both theoretical and applied aspects). Tutorials will be given by world experts: David Blei (Columbia), Richard Nickl (Cambridge), Aad van der Vaart (Leiden), and Cun-Hui Zhang (Rutgers). Young researchers will also be given the opportunity to present their work in the format of contributed talks or posters. Location: Eindhoven, the Netherlands Website: http://www.eurandom.nl/events/workshops/2017/YES_VIII
6-8 Feb	*5th Workshop on Probabilistic and Statistical Methods* The Workshop on Probabilistic and Statistical Methods is an initiative of the Programa Interinstitucional de Pós-graduação em Estatística (PIPGEs ICMC/USP and UFSCar), which brings together the Statistics and Probability research groups from ICMC/USP and UFSCar, at São Carlos, SP, Brazil. This meeting intends to discuss new developments in Statistics, Probability and their applications. Activities include invited plenary sessions, short talks, one poster session and one minicourse. The topics of this meeting include Probability and Stochastic Processes, Statistical Inference, Regression Models, Survival Analysis and Complex Stochastic Systems. The aim of the workshop is to provide a unique opportunity for researchers and students to exchange experiences and start collaborations. Location: São Carlos, SP, Brazil E-mail: Juliana Cobre at jucobre@icmc.usp.br or Renato Gava at gava@ufscar.br Website: http://estatisticaverao.icmc.usp.br/wpsm_en.html
9-11 Mar	*II Latin American Conference on Statistical Computing* he purpose of the II LACSC is to bring together researchers that use computational statistical methods, to share and discuss ways to improve the access to knowledge, and promote interdisciplinary collaborations. The scientific program will be very appealing for most statisticians and other researchers interested in computational methods and data analysis, and will include invited paper sessions, contributed paper sessions and contributed posters. Location: Valparaíso, Chile E-mail: lacsc@usm.cl Website: http://www.lacsc.mat.utfsm.cl/
5-6 Apr	*Survival Analysis for Junior Researchers 2017* This two day event is aimed at career-young statisticians with an interest in the application and development of time-to-event analysis and related topics. The conference provides a unique opportunity for participants to present and discuss their work with peers at a similar stage in their careers in a relaxed and friendly environment. The event further includes talks from keynote speakers, Prof Per Kragh Andersen (University of Copenhagen), Dr Therese Andersson (Karolinska Institutet) and Dr Nick Latimer (University of Sheffield) as well as poster sessions and an evening social event. Location: Leicester, UK Email: safjr2917@le.ac.uk Website: http://www2.le.ac.uk/departments/health-sciences/research/biostats/survival-analysis-for-junior-researchers-2017
24-26 Apr	*2017 Channel Network Conference* For your information, the 2017 Channel Network Conference of the International Biometric Society (IBS) will take place at UHasselt (Belgium) from Apr 24 until Apr 26. This biennial conference, organized by IBS regions Belgium, France, Great-Britain/Ireland and The Netherlands, aims at gathering biostatisticians to discuss the newest methodologies for the analysis of biological and medical data. Location: Hasselt, Belgium E-mail: info@ibschannel2017.be Website: http://www.uhasselt.be/channel-network-conference-2017
8-12 May	*Eastern Mediteranean region IBS conference* The 9th EMR-IBS conference will be organized jointly with the Italian Region in Thessaloniki, Greece. The meeting is devoted to the memory of Prof . Marvin Zelen. Note that the weekend before the conference there will take place at the same venue the Symposium honoring Marvin Zelen, (6-7 May 2017) organized by Frontier Science Hellas and Frontier Science Foundation. Location: Thessaloniki, Greece E-mail: emr2017@pco-convin.gr Website: http://www.stat-athens.aueb.gr/~emribs/page/emr2017.html
20-23 Jun	*10th International Conference on Multiple Comparison Procedures* The 10th International Conference on Multiple Comparison Procedures (MCP) will be held on the campus of the University of California, Riverside. Now in its twentieth year, the biennial MCP conference promotes fundamental research and application of MCP and provides a unique forum for interactions among industry practitioners, research scientists from subject matter areas and statisticians. This unique conference continues the dialogue among academia, industry and regulatory agencies to explore innovative solutions for statistical challenges and their applications in modern scientific investigations including those in clinical trials, drug discoveries and bioinformatics/genomics. Sessions will include theory and applications in closed testing, multiple endpoints, adaptive designs, group sequential designs, subgroup analysis, post selection inference and new multiple testing approaches to foster future advances in the field. Location: Riverside CA, USA E-mail: xinping.cui@ucr.edu Website: http://www.mcp-conference.org/
25-28 Jun	*37th International Symposium on Forecasting* The International Symposium on Forecasting (ISF) is the premier forecasting conference, attracting the world's leading forecasting researchers, practitioners, and students. Through a combination of keynote speaker presentations, academic sessions, workshops, and social programs, the ISF provides many excellent opportunities for networking, learning, and fun. Location: Cairns, Australia E-mail: forecasters@forecasters.org Website: https://forecasters.org/isf/
3-7 Jul	*ICORS 2017* The aim of the International Conference on Robust Statistics (ICORS) is to bring together researchers and practitioners interested in robust statistics, data analysis and related areas. This includes theoretical and applied statisticians as well as data analysts from other fields, and leading experts as well as junior researchers and graduate students. Location: Wollongong, Australia E-mail: icors2017@uow.edu.au Website: http://niasra.uow.edu.au/icors2017/index.html
9-13 Jul	***38 Annual Conference of the International Society for Clinical Biostatistics*** **The International Society for Clinical Biostatistics (ISCB) was founded in 1978 to stimulate research into the principles and methodology used in the design and analysis of clinical research and to increase the relevance of statistical theory to the real world of clinical medicine (moreinfowww.iscb.info). Like previous annual conferences of ISCB the 2017 conference will provide a scientific forum for international exchange of theory, methods and applications of biostatistics in medical research and practice among clinicians, statisticians and members of other disciplines, such as epidemiologists, clinical chemists and clinical pharmacologists, working or interested in the field of clinical biostatistics. Location: Vigo, Spain Website: http://iscb2017.info/ E-mail: iscb2017@orzancongres.com**
16-21 Jul	**International Statistical Institute, *61st ISI World Statistics Congress*** Includes meetings of the Bernoulli Society, the International Association for Statistical Computing, the International Association of Survey Statisticians, the International Association for Official Statistics, the International Association for Statistics Education, the International Society for Business and Industrial Statistics, and The International Environmetrics Society. **Location:** Marrakesh, Morocco **Information:** ISI Permanent Office, P.O. Box 24070, 2490 AB The Hague, The Netherlands. **E-mail:** Contact **Phone:** +31–70–3375737 **Fax:** +31–70–3860025 **Website:** www.isi2017.org/
7-9 Sep	*GEOMED 2017* The Institute for Research and Innovation in Health (Instituto de Investigação e Inovação em Saúde, i3S) is pleased to announce GEOMED 2017-"Deeper insight from big data and small areas". GEOMED 2017 is the international interdisciplinary conference on spatial statistics, geographical epidemiology and geographical aspects of public health. This conference will be held in Porto, Portugal, from 7 to 9 Sep 2017 and aims to bring together statisticians, geographers, epidemiologists, computer scientists and public health professionals to discuss spatial and spatio-temporal methods in health studies. Some of the most international recognized scientists in the area of spatial analysis in health have already confirmed their participation, among them Ana Diez Roux, Allison Lieber, Andrew Lawson, Daniel Griffith, David Martin, Duncan Lee, Giovani L Silva, Jamie Pearce, Jon Wakefield, Marilia Carvalho, Peter Diggle, Pietro Ceccato, Rachel Lowe, Renato Assunção, Robert Hainning and Trevor Bailey. Location: Porto, Portugal E-mail: rita.matos@i3s.up.pt Website: http://www.i3s.up.pt/geomed2017/index.html
2018: 26-30 Aug	*Joint Conference of the International Society for Clinical Biostatistics and the Statistical Society of Australia* The International Society for Clinical Biostatistics (ISCB) was founded in 1978 to stimulate research into the principles and methodology used in the design and analysis of clinical research and to increase the relevance of statistical theory to the real world of clinical medicine (more info www.iscb.info). The Statistical Society of Australia was founded in 1962 to encourage the study, application and good practice of statistical theory and methods in all branches of learning and enterprise (www.statsoc.org.au). This joint conference will provide a scientific forum for international exchange of theory, methods and applications of statistics. Location: Melbourne, Australia E-mail: iscbasc2018@arinex.com.au Website: www.isbcasc2018.com
2019: 14-18 Jul	*40th Annual Conference of the ISCB* The International Society for Clinical Biostatistics (ISCB) was founded in 1978 to stimulate research into the principles and methodology used in the design and analysis of clinical research and to increase the relevance of statistical theory to the real world of clinical medicine. Like previous annual conferences of ISCB, the 2019 conference will provide a scientific forum for international exchange of theory, methods and applications of biostatistics in medical research and practice among clinicians, statisticians and members of other disciplines, such as epidemiologists, clinical chemists and clinical pharmacologists, working or interested in the field of clinical biostatistics. Location: Leuven, Belgium E-mail : tomasz.burzykowski@uhasselt.be Website: www.iscb.info
2020: Aug	**ISCB41. Krakow, Poland**
2021+:	**ISCB42, 43… ?** **ISCB is looking for enthusiastic local organisers of conferences from 2021 onwards. If you would like to know more about what this involves, please contact any of the ISCB Officers, ExCom or SCs who can let you more about what has to be done, when.** **Initial proposals for 2021should be sent to the Officers by 01 Jun 2017 at the latest.**